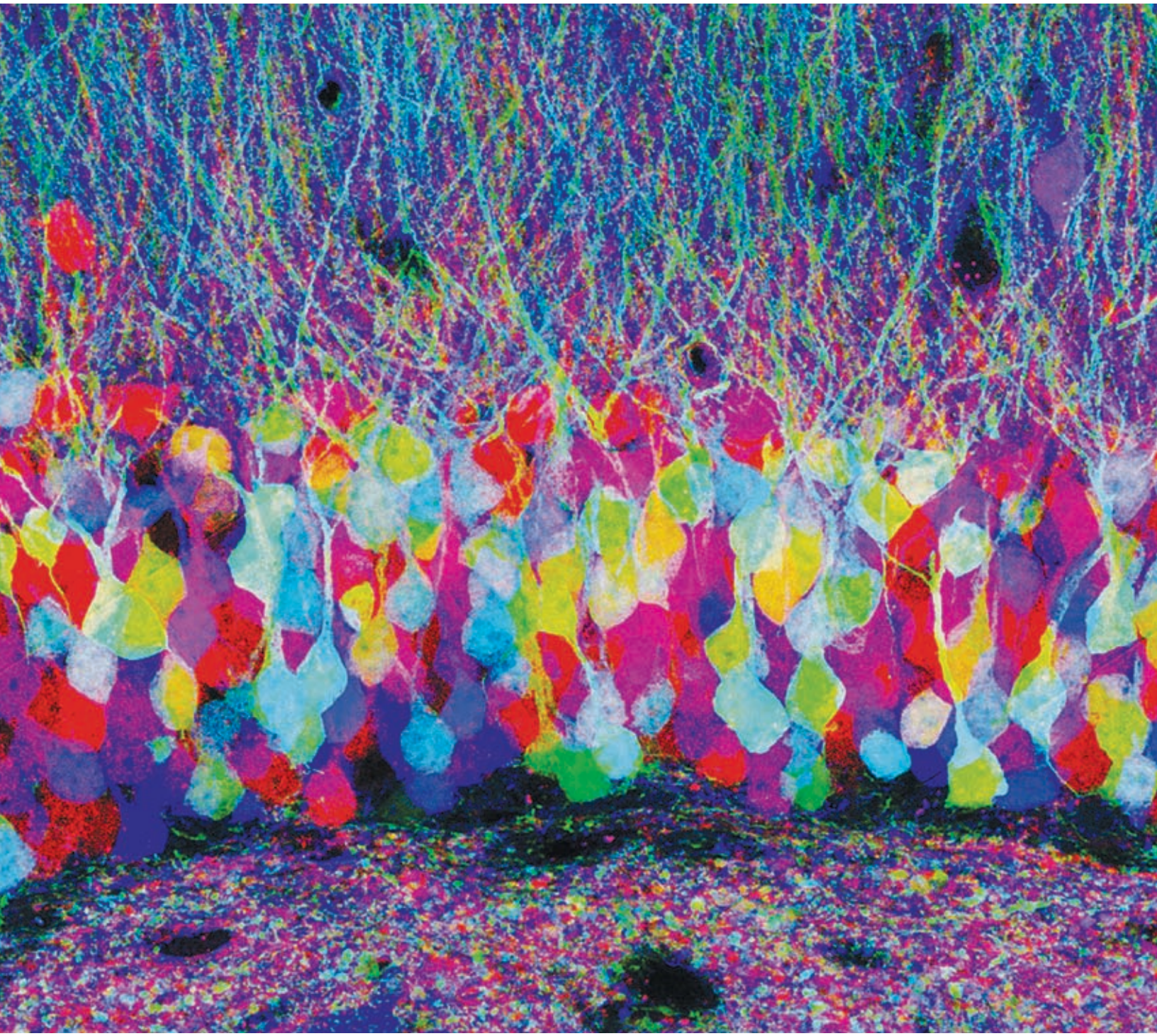
California Biomedical Industry

2009 Report



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California Healthcare Institute

PricewaterhouseCoopers

Contents

Cover image: Neurons labeled in the dentate gyrus of JAX Mice strain B6;CBA-Tg(Thy1-Brainbow1.0)LLich/J (Stock Number 007910) (recombination with CreERT2). Livet et al., Nature 450: 56 (2007).

Image courtesy of Dr. Jean Livet, Harvard University.

Letter from the Governor

GOVERNOR ARNOLD SCHWARZENEGGER

2009

California Healthcare Institute

California is proud of our fantastic biomedical industry and the incredible influence it has on our state and world. Thanks to the outstanding men and women who have devoted their lives to advancing medicine, countless patients around the globe are receiving new treatments, better care and hope for a healthier future.

My gratitude goes to your members and all those who are taking action to support the research and policy efforts that will help us take huge leaps in our understanding of the human body and the diseases that affect us. Your dedication also means our biomedical industry touches many lives through the jobs it creates for hard working Californians. Thank you for your commitment to supporting an industry that plays such an important role in the lives of countless people.

Again, I offer my deepest appreciation for your efforts, and I reaffirm my commitment to making sure that our state remains a trailblazer in the biomedical industry. I have no doubt that with your help California will continue to lead the world in discoveries, treatments and cures.

Sincerely,

Arnold Schwarzenegger

STATE CAPITOL · SACRAMENTO, CALIFORNIA 95814 · (916) 445-2841

Letter to our Stakeholders
January 2009

David L. Gollaher, Ph.D.

We enter 2009 amidst unprecedented turbulence in the world's financial markets and historic change in American government. And the 2008 elections, in which for both major parties the operative word was "change," left no doubt just how directly the economic crisis is linked to politics. Both factors, financial and political, are transforming the environment for biomedical research and innovation. Constrained capital markets make it more difficult than ever to attract funding for biopharmaceutical and medical technology firms. Government budgets at the federal and state levels face staggering deficits along with pressure to slash spending on entitlement programs. Meanwhile, in reaction to what many see as excesses of unbridled capitalism, the 111th Congress and Obama administration promise stronger federal regulation and a far more aggressive government role in the nation's healthcare economy.

The group portrait illustrated in this report suggests that California's biomedical industry should be a key part of the state's economic recovery. Altogether, life sciences companies and academic institutions directly employ some 271,000 Californians, making our sector the state's second leading source of high-tech jobs (just behind information technology products and services). There is also a multiplier-effect; for each direct job, another three to five people provide the industry with services, support and products. So our full employment footprint almost certainly includes more than one million workers. Within the biomedical industry proper, annual wages average nearly $75,000. As a whole, in 2007 it generated almost $75 billion in revenues.

Tracy T. Lefteroff

Industrialized nations around the world–and most of the 50 states–are striving to attract life sciences companies. This is primarily because they create high-value intellectual property, encourage the development of an educated workforce, manufacture products for export, and ultimately do all this while preserving the environment. There's another reason, too. Biomedicine, after all, is the only hope for many of the world's worst diseases. Cancer, Parkinson's, Alzheimer's–there is a long list of disorders, which have no hope of effective treatment or cure except from scientific breakthroughs that can be transformed into products for patients.

Historically the biomedical business model worked as follows. Academic scientists discovered an invention, say, a novel way of genetically engineering a crucial human hormone. In turn, the inventors collaborated with venture capitalists, who put up seed money to found a company and hire a team who could do the essential development work and negotiate the tortuous path from laboratory discovery through regulatory review at the U.S. Food and Drug Administration (FDA). Typically things turned out to be more complicated, thus more time-consuming and more costly, than originally projected. Still, if the technology were promising, the company would enjoy an opportunity to float an initial public offering (IPO), raising money by selling shares in the stock market. In the best cases, as with Genentech, Amgen and Gilead, after investing many hundreds of millions, companies launched successful products that both saved lives and richly rewarded their investors.

The financial and political upheavals of 2008-09 pose distinct challenges to this model. At its most basic level, the financial crisis reflects deleveraging and a global reevaluation of risk. This has profound implications for the biotechnology industry, which from inception has been characterized by high risks and high rewards. As investors across the spectrum—from institutions to venture capitalists to individuals—try to squeeze risk out of their portfolios,

less capital is available for early-stage companies with unproven science or uncertain paths to market. The difficulty of attracting risk capital into biotech is compounded by today's aversion of the public stock markets to IPOs. Absent the opportunity to take companies public, early investors have limited opportunities to capture returns on their capital. In the days ahead, the financial model for biomedical companies will adjust to these new financial realities. But this is likely to mean serious consolidation, with smaller, cash-strapped companies being acquired by larger players, and venture investments flowing toward fewer start-ups and more proven businesses.

At the same time, even as the recession has eroded government's revenue base and brought record deficits, congressional leaders and the president are focusing on healthcare reform with new energy. Specific challenges the biomedical industry will confront in healthcare reform depend on the scope and scale of legislation. Will reform be a sweeping effort toward universal coverage, or a set of incremental steps to improve coverage and rein in Medicare and Medicaid spending? In either case, though, the industry is likely to see early action on certain issues.

- Legislation authorizing the FDA to create a regulatory pathway for the approval of follow-on biologic drugs. How this balances the objectives of patient safety, increased price competition and sufficient incentives for future investment in innovation will shape the future of biotech.

- Comparative effectiveness research. The Congressional Budget Office has maintained that the main driver of high healthcare costs is advancing medical technology. Congress is likely to create a government-sponsored institution to produce health technology assessments. Its structure, mission and operations are of great concern to the producers of medical innovation.

- Stem cell research and National Institutes of Health (NIH) funding. While congressional leadership and President Obama support easing restrictions on stem cell research, the federal budget deficit places severe pressure on federal research funding.

- FDA preemption. Legislation that would remove federal preemption in product liability lawsuits for medical device manufacturers was introduced in 2008. It will certainly be reintroduced, perhaps in expanded form to include drugs, in the 111th Congress.

- Marketing practices and conflicts of interest. The regulatory bent of Congress (and state legislatures) to restrict financial arrangements between physicians and industry gained momentum in 2008.

For the biomedical industry, the next chapter in the story told in these pages will depend partly on the recovery of the financial markets, and their ability to sustain the next cycle of risk investment, and partly on the industry's ability to work with policymakers to craft policy solutions to real cost and access problems that face the nation.

David L. Gollaher, Ph.D.
President and Chief Executive Officer
California Healthcare Institute

Tracy T. Lefteroff
National Life Sciences Partner
PricewaterhouseCoopers LLP

Defining the California Biomedical Industry

California's biomedical industry has grown organically from ideas first germinated in the state's universities. Through technology transfer, entrepreneurial commitment and investor financing, basic science discoveries have led to breakthrough technologies to better understand, diagnose, treat and cure a broad range of medical disorders.

This organic growth has spawned vibrant biomedical clusters in California. The oldest and largest is in the San Francisco Bay Area. This region, with its world-class universities and life sciences firms, is recognized as a leading center for biotechnology, biopharmaceutical and genomics innovation. In Southern California, the San Diego cluster is renowned for its biopharmaceutical and diagnostics enterprises. Orange County has been called the epicenter for medical device inventions. And the Los Angeles basin is growing its reputation as an oncology research center based on work at City of Hope, UCLA, Caltech, and Cedars-Sinai Medical Center, among others.

Altogether, the clusters and other biomedical companies in California employ approximately 271,000 people in more than 2,000 companies. Moreover, for every individual directly employed by biomedical organizations there is a multiplier effect, with another three to five people employed in firms that offer goods and services—from lab supplies to construction and accounting—to the industry.[1]

With respect to the revenue base of academic institutions, their activities are mainly funded by government grants. California continues to secure the largest share of NIH funding among the states, with $3.2 billion awarded here in 2007. These funds are increasingly more difficult to acquire, however, as the NIH budget is under pressure and competition for grants is more fierce than ever.

Before mid-2008, investments by venture capitalists and the equity markets continued to represent key sources of revenues for start-up and emerging companies. California life sciences companies attracted $4.3 billion in venture capital investment in 2007. During that year, 11 U.S. VC-Backed biotechnology companies issued IPOs and raised $679.2 million in the process. In contrast, no biomedical IPOs were completed in 2008 and no IPOs in other industries were issued after August 2008. On November 30, 2008, California's 102 NASDAQ-listed biomedical companies' combined market capitalization totaled $131 billion, and comprised nearly 34 percent of the market cap for all the NASDAQ-listed healthcare companies.

For established biomedical companies, the largest source of revenue derives from product sales, although grants, contract research fees and milestone payments also fall in this category. Taken together, California-based life sciences firms generated $74.5 billion in revenues in 2007, more than $35 billion of that in global pharmaceutical sales.

Still, the picture of the industry suggested by theses figures describes a period of past prosperity. The present and immediate future are far more grim. The meltdown of the global credit markets, beginning in September and October 2008, roiled the biomedical industry. Stock prices of public companies fell sharply, so companies found themselves unable to raise capital through secondary

2009 California Biomedical Industry Report Highlights

Number of California biomedical companies: 2,042

Total estimated revenues: $74.5 billion

Total estimated employment: 271,000

Total estimated wages and salaries paid: $20.3 billion

Average wage: Nearly $75,000

Total NIH grants awarded: $3.2 billion

Total estimated venture capital investment in California biomedical companies: $4.3 billion

offerings. Tight credit meant that traditional avenues of borrowing money—bonds, convertible debt, and so forth—were closed. Particularly vulnerable were development-stage firms whose products remained in some stage of clinical trials. Unless these companies had ample cash reserves to fund their research, they risked being acquired at substantial discounts or, worse, going out of business. Even the largest and most profitable pharmaceutical and medical device manufacturers began to trim operations, cutting costs wherever possible, and limiting their strategic investments in smaller firms. Government grants, given the country's record deficit and the pressing priorities facing the incoming administration, are expected to become more difficult to secure, too.

In the face of a serious recession—and a new administration focused on reining in healthcare costs—there is great interest in adopting comparative effectiveness research, limiting intellectual property protections and using government power to control the cost of medical technologies. Those factors alter the risk-reward calculus of pursuing new products and, thus, dampen innovation. At the same time, consumers are anxious about the security of their jobs, mortgages and retirement savings and are cutting back wherever they can. Discretionary spending on healthcare—from LASIK surgery to cosmetic pharmacology to preventive medicines—is under pressure from falling consumer confidence.

While the immediate loss of market value and impact of tight credit is painfully apparent, the long-term impact of the present financial crisis is impossible to predict. Like the automotive industry in Michigan and the financial services sector in New York, high-tech industries are a vital engine driving California's economy and future. This report helps outline what the biomedical industry could deliver to the state, given critical support through the coming months and years.

1. DeVol R, Wong P, Ki J, Bedroussian A, and Koepp R. *America's Biotech and Life Sciences Clusters: San Diego's Position and Economic Contributions.* Milken Institute. June 2004. Accessed at: http://www.milkeninstitute.org/pdf/biotech_clusters.pdf

Industry Sectors

The California biomedical industry encompasses several sectors focused on improving public health, human medicine and the quality of life for patients around the world.

Academic research: Scientific exploration in California's universities and public and private research centers leads to discoveries that frequently enter the commercial biomedical industry through technology transfer. Such transactions can include contract research, licensing agreements and spin-off companies.

Biopharmaceuticals: This category captures companies whose biologics or bioengineered products are produced by altering or replicating proteins (including antibodies) or nucleic acids (DNA, RNA or antisense oligonucleotides) for therapeutic or diagnostic purposes. It also includes companies developing small-molecule drugs to be manufactured from chemical compounds.

Diagnostics: This category encompasses technologies that analyze biologic samples for medical purposes. Examples include magnetic resonance imaging scanners in hospitals, tests used to keep the blood supply safe and such over-the-counter products as home pregnancy tests. Diagnostics are also a key component in biomedical research and include reagents, cell analysis instruments, high-throughput screening devices and every imaginable instrument vital to science.

Medical devices: Encompassing all mechanical means for improving or diagnosing human health and mobility, medical devices can be further sorted into two general categories. Instruments include tools used by medical professionals in their work. Examples include scalpels, lasers and heart monitors. Implants are medical devices, such as artificial hips or heart valves, that are surgically placed to perform a function that the body cannot provide or adequately perform for itself.

Laboratory services: Laboratories that test patient or research samples use highly technical, precisely calibrated and strictly regulated equipment and procedures to ensure accurate results.

Wholesale trade: Managing the import, export and exchange of pharmaceuticals, medical devices, diagnostics and research reagents and other supplies, wholesale trade companies are an important segment of California's biomedical industry.

Employment

The global economy enters 2009 under unprecedented pressure. The world's governments, businesses, investors and citizens are watching the markets with concern to see how the international financial crisis will be resolved. This anxiety is shared among California's biomedical companies and academic research institutions, which rely heavily upon the capital markets and government grants and philanthropy. Many California researchers, innovators and entrepreneurs work for organizations that count their funding in "months remaining." At press time, it remains unclear how deep the financial crisis will cut, how many projects might be shelved, indeed, how many enterprises may ultimately fail before the economy recovers.

Yet, despite the marketplace's malaise, the innovators and investors in the Golden State's life sciences and medical technology sectors are committed to commercializing new products and therapies to improve public health and patients' lives. They fully appreciate how much unmet medical need remains in the world. They see aging populations and growing burdens of chronic and infectious diseases. They remain optimistic that their breakthrough discoveries will continue to lead the world's scientific and technological advances, and benefit humankind for generations to come. And they continue to nurture the best and brightest in California.

As the following data show, California has built a workforce and industry that is vital both to the world's health as well as to the state's economy and continued leadership role in scientific, engineering and medical excellence.

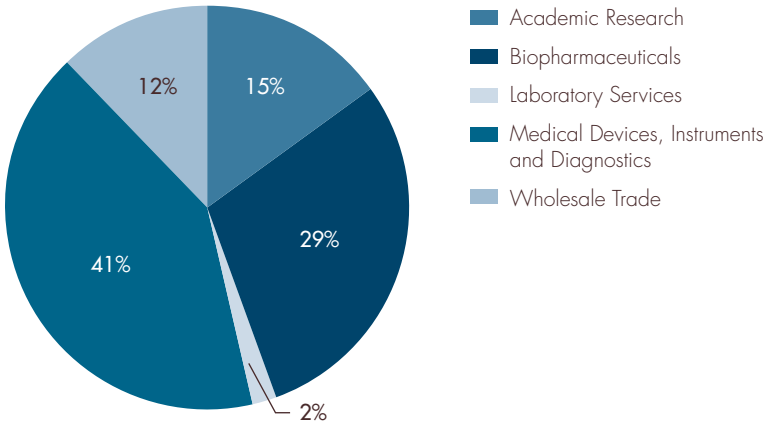
Jobs

In 2007, the biomedical industry employed approximately 271,000 Californians (Figure 1). Employers in the medical devices, instruments and diagnostics sectors accounted for approximately 112,000, or about 41 percent of the overall total. Biopharmaceutical companies employed the next-largest segment with nearly 80,000 or about 29 percent. The state's academic research centers employed about 42,000 people in life sciences positions for approximately 15 percent of the total. Wholesale trade accounted for over 32,000 personnel or about 12 percent of the state's biomedical employees. The laboratory services sector rounded out the overall industry with approximately 5,200 employees or about 2 percent.

Geographically speaking, biomedical industry jobs draw workers from all over California (Figure 2). The largest concentration of industry-related jobs is centered in the San Francisco Bay Area. Companies and academia there employ nearly 50,000 people or more than 18 percent of the state's total. San Diego, Riverside and San Bernardino counties were home to

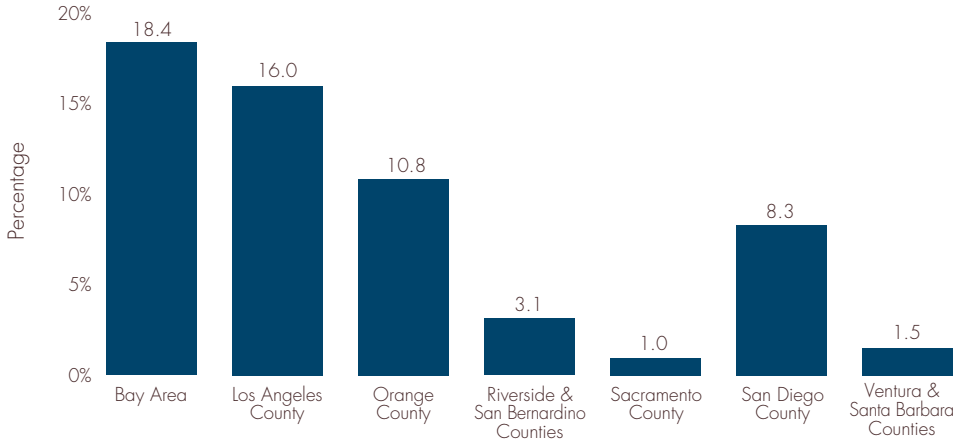
approximately 31,000 biomedical employees or 11 percent of the total in 2007. Los Angeles County companies and institutes employ more than 43,000 people or approximately 16 percent, and Orange County encompasses nearly 29,000 or about 11 percent. The remaining 86,000 or 32 percent of California's biomedical employees work at companies or institutions outside of the concentrated clusters.

Figure 1: Distribution of employment in California's biomedical industry by sector, 2007



Note: Numbers may not sum to total due to rounding
Source: California Employment Development Division Bureau of Labor Statistics and company-specific SEC filings.

Figure 2: Distribution of employment in California's biomedical industry by geographic cluster, 2007



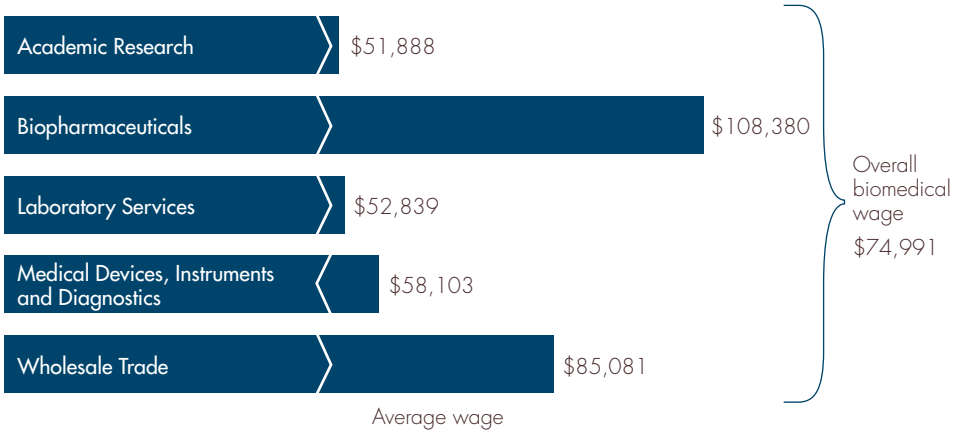
Source: California Employment Development Division Bureau of Labor Statistics and company-specific SEC filings.

Wages

In 2007, California biomedical industry employees earned a total of $20.3 billion. For the year, the average annual wage for the industry across the state was nearly $75,000, up approximately 9 percent from 2006.

The averages continue to vary among the industry's sectors (Figure 3). Biopharmaceutical companies pay the highest average annual wages, with 2007's mark reaching approximately $108,000. Wholesale trade came in second with average annual wages of about $85,000. Academic research, laboratory services and medical device organizations paid salaries in the low- to high-$50,000 range. The variances in compensation are attributable in part to differences in required education and training and in the commercial success of the various sectors.

Figure 3: Estimated average annual wage, by sector, 2007

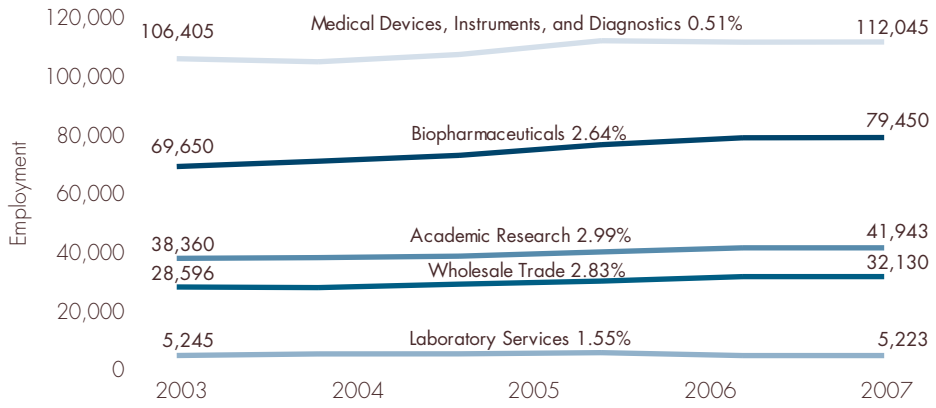


Note: 2006 wages inflated to 2007 using the Consumer Price Index
Source: Bureau of Labor Statistics

Trends

In 2007, California's biomedical industry continued to add jobs (Figure 4). Between 2003 and 2007, the industry added approximately 23,000 jobs and grew at an annual average rate of 1.76 percent. Each segment increased its overall employment levels, although the growth rates varied among the biomedical industry sectors. Biopharmaceutical employment expanded at an average annual rate of 2.64 percent, year-over-year while laboratory services grew at the slower pace of 1.55 percent 2006-2007.

Figure 4: Employment in California's biomedical industry, 2003–2007

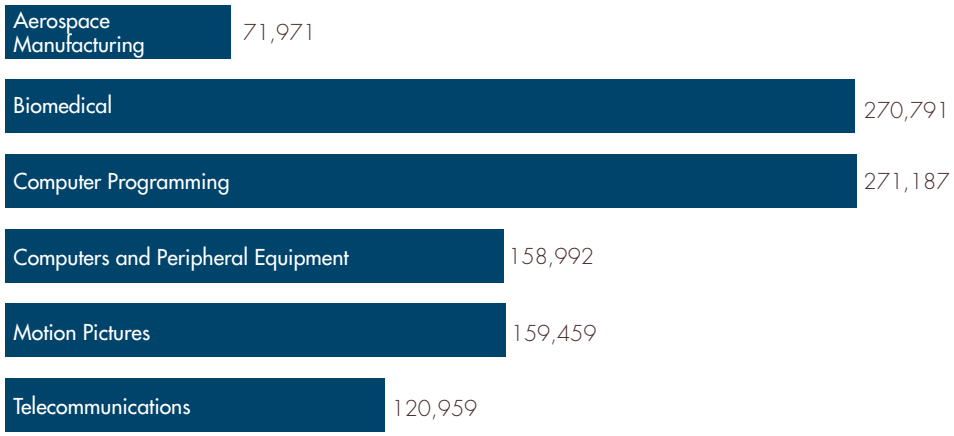


Source: California Employment Development Division, Bureau of Labor Statistics, and company specific SEC filings.

Context

California is known for its high-tech industries and among those industries, the biomedical and computer programming sectors employ the most people. Both industries employed roughly 271,000 people in the Golden State in 2007 (Figure 5).

Figure 5: Estimated employment in California's high-tech industries, 2007

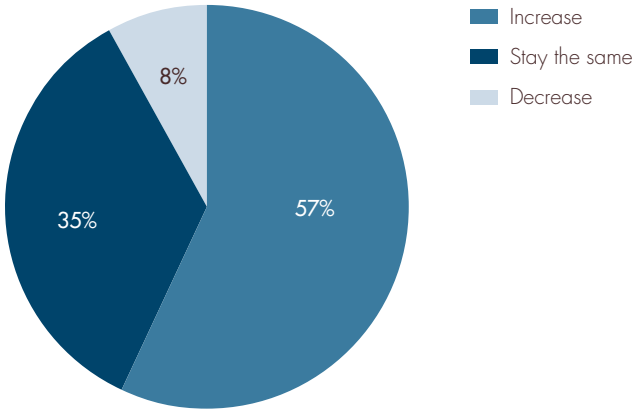


Souce: California Employment Development Division, Bureau of Labor Statistics

Expectations

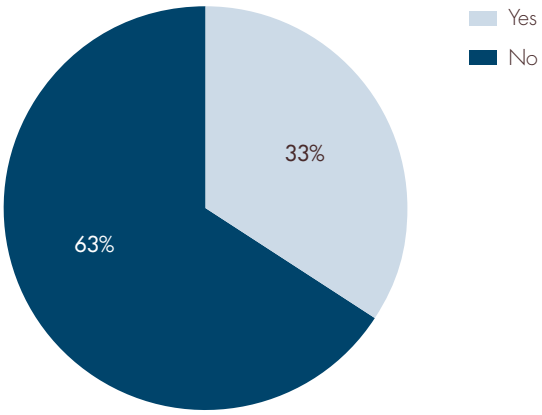
Biomedical companies responding to the CHI-PricewaterhouseCoopers survey continue to remain committed to their California operations and personnel. The survey, completed in late fall 2008, showed that 57 percent intended to increase their headcounts over the coming year, with only 8 percent anticipating reductions in staff.

Figure 6: CHI-PwC Survey: In the next year, how does the company expect its overall workforce headcount to change within California?



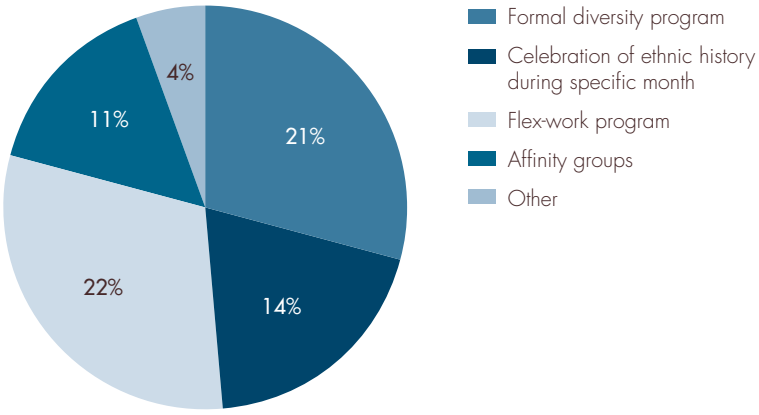
The biomedical industry is committed to diversity in the workplace. A third of respondents have provided programming specifically to encourage diversity within their companies.

Figure 7: CHI-PwC Survey: Did the company provide any programming to encourage or promote diversity within the company itself?



Those companies offering diversity programs approached the task from multiple directions. Included in their effort were ethnic celebrations, flex-work programs and affinity groups, as well as formal diversity programs.

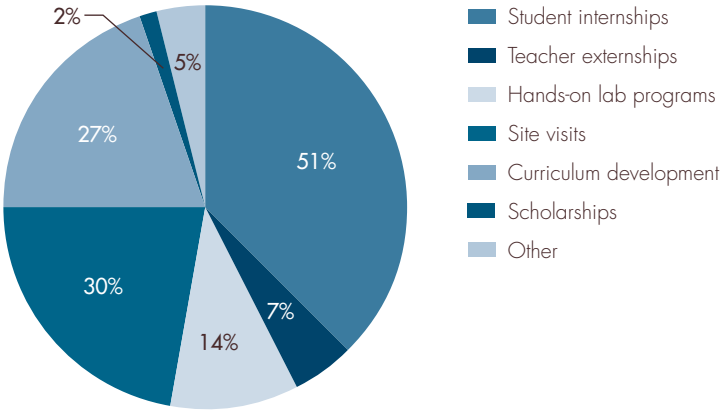
Figure 8: CHI-PwC Survey: What type(s) of diversity program(s) has the company implemented?



Note: Numbers may not sum to total due to rounding

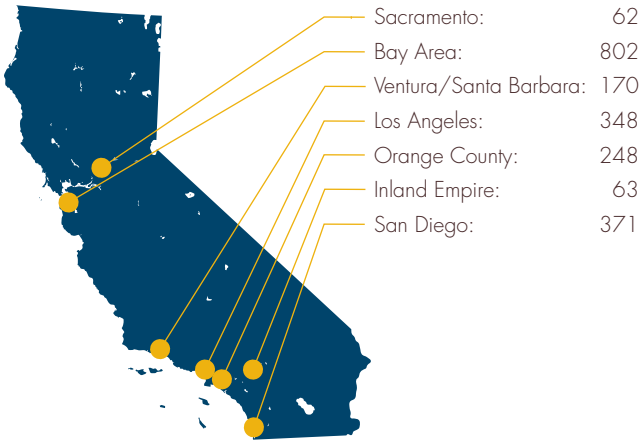
Attention to diversity issues within workforce development is also important to the biomedical industry in California. More than half of respondents offered student internships and their involvement in training and education ran the gamet from curriculum development and teacher training to site tours and hands-on lab programs.

Figure 9: CHI-PwC Survey: Did the company offer programs encouraging workforce diversity within the community or outside of the company?



Note: Numbers may not sum to total due to rounding

Figure 10: Employment Opportunities in the Biomedical Industry in California



Source: Job listings from Monster.com as accessed on Dec. 10, 2008

Although the current financial climate in California appears grim, 57 percent of respondents to CHI/PWC's survey expected to increase headcounts. Figure 10 shows employment opportunities in the industry in each cluster.

Industry-Supported Programs to Improve STEM Education and Diversity

A number of organizations throughout the United States are working together to excite young people about science, technology, engineering and mathematics (STEM) education opportunities—and the careers for which that training could prepare them. Recognizing that future growth, success and products depend on quality STEM education today, California's biomedical companies are committed to supporting and developing learning opportunities for the Golden State's students. Among such programs are:

- Amgen Scholars
- Bayer's Making Science Make Sense
- Biogen Idec Community Lab
- Biotech Partners
- Cedars-Sinai Youth Employment and Development Program
- Discovery Science Center
- Elementary Institute of Science
- Eugene and Ruth Roberts Summer Student Academy
- Genentech Foundation
- Genentech Foundation for Biomedical Sciences
- High Tech High
- Inner World Discovery
- Life Sciences Summer Institute
- Pfizer Education Initiative
- Preuss School
- Science Matters
- Skyline College Biomanufacturing Training Partnership
- United Negro College Fund/ Merck Science Initiative
- Alliance/Merck Ciencia Hispanic Scholars Program
- Merck Index Women in Chemistry Scholarships

Ted W. Love, M.D.

PROFILE

Ted W. Love, M.D., has been Nuvelo, Inc.'s chief executive officer and chairman of the board since 2001 and 2005, respectively. The company is in the process of merging with ARCA Biopharma, Inc. Prior to joining Nuvelo, Love was senior vice president of development at Theravance Inc. and a research physician and vice president of product development at Genentech. After earning his bachelor's degree in molecular biology from Haverford College and his medical degree from Yale Medical School, Love completed his residency and fellowship training in internal medicine and cardiology at Massachusetts General Hospital and Harvard Medical School.

In 2001, Ted W. Love, MD, joined a turn-around team that created Nuvelo and grew it into a company with a $1 billion market cap. Nuvelo in-licensed a compound from Amgen and began developing it for leg clots, stroke and occluded catheters. The executive team raised nearly a quarter of a billion dollars and forged a partnership with Bayer on its lead product.

Unfortunately the compound failed in clinical trials. Nuvelo lost its deal with Bayer, its stock price plummeted, and Love had to oversee two rounds of lay-offs. At the end of September 2008, Nuvelo announced its merger with a Colorado company.

Such are the reversals of fortune in the biopharmaceutical industry. Yet Love focuses on the positives: Nuvelo's remaining capital and expertise will be leveraged to move ARCA's lead drug candidate, Gencaro*, to market. Gencaro is a genetically-targeted beta-blocker with unique vasodilating properties for the treatment of heart failure. Approval could come in mid 2009 with product launch in 2010. ARCA also will drive further development of Nuvelo's lead candidate, a short-acting anticoagulant being tested as a potential new therapy in coronary artery bypass graft (CABG) surgery, kidney dialysis and a variety of vascular surgical and coronary interventions. The merger "puts shareholders back into position to regain their value," Love said.

"This is a business for optimists," Love said, and he remains optimistic about the future of the biomedical industry. "This is an industry of smart, hard-working, risk-taking people, particularly in California…the ethos here generated the Amgens, Genentechs, Googles, Yahoos, and eBays of the world. That's not going to stop. I can't imagine that California is ever going to dry up as a source for new ideas."

While Love is looking forward to his first break since entering medical school, he said he would not change any of his career choices. "I really loved the process of learning medicine," he said. "It was a privilege to get into a position to understand the science. What pulled me into biotech was the excitement that I could put that information and training to work in a different arena." He said, "It's just phenomenal to get up and go to work and to work on projects that will change the lives of patients."

*Trade name pending FDA approval.

City of Hope Provides Hands-On Learning Experiences

The Eugene and Ruth Roberts Summer Student Academy program, established in 1975 by City of Hope's director emeritus of neurobiology, Eugene Roberts, Ph.D., gives promising students with an interest in research and health science careers practical experience and helps them develop important skills for their futures. Unlike traditional high school or college classes in which the course of study is entirely determined by the instructor, City of Hope's summer program students select their own research project according to their individual areas of interest. City of Hope's own chief medical officer, Alexandra Levine, M.D., is a Summer Student Program alumna, as are many prominent scientists in academia and industry.

The primary goal of the Eugene and Ruth Roberts Summer Student Academy is to provide high school and university students with an opportunity for a "hands-on" research experience. Another goal inherent to City of Hope's mission is to promote translational research: applying exciting research discoveries to patient clinical trials. The students participating in the program gain exposure to this approach daily, and it helps them to develop into full-fledged researchers and physicians.

The instructors leading the program are world-renowned physicians and scientists who guide students in their research, while helping them develop their critical thinking skills. Weekly seminars during the 10-week program allow students to present research findings to their peers, a good primer for what graduate and postdoctoral students do. There are workshops covering topics such as creating posters for research talks, biomedical ethics and other important subjects. Students interact with their peers and their research directors on a continual basis, fostering valuable relationships for the future. Summer program participants also receive a stipend of $4,000 for their work.

Additionally, as a National Cancer Institute-designated Comprehensive Cancer Center, City of Hope is proud to be part of the Continuing Umbrella of Research Experience (CURE) Program, which is designed to engage the scientific curiosity of promising young high school and undergraduate students from underrepresented populations who are interested in cancer research as a career. Underrepresented populations in the program include African-American, Hispanic, American Indian, and Pacific Islander. CURE students work side by side with City of Hope scientists on current, challenging research projects. The CURE Program lasts 12 weeks.

Martha A. Ornelas

PROFILE

Martha A. Ornelas is a chemist at Pfizer's research and development facility in La Jolla, Calif. She earned her bachelor's degree in biopharmaceutical chemistry from the Autonomous University of Baja California. She taught undergraduate basic and organic chemistry at her alma mater for eight years before volunteering at the San Diego State University lab of Dr. Sam Somanathan. From there, she joined biotech start-up Agouron Pharmaceuticals, which was bought by Warner-Lambert in 1999 and then Pfizer in 2000.

Martha A. Ornelas is a member of the Pfizer Inc discovery team, which is working on early discovery oncology projects. "Once a 'drug-able' target is identified," she says, "a multidisciplinary team of scientists decides which series of compounds could be good ligands for that particular protein." The team's chemists design the targeted compounds, and Ornelas helps synthesize, purify and characterize the new chemical entities. She also is involved with the design and synthesis of compound libraries for further screening.

Ornelas joined Pfizer as a temporary employee eight years ago when Agouron's parent, Warner-Lambert, merged with Pfizer. She said that she knew within six months that it was the perfect job for her. "The everyday challenges were and still are a constant stimulation for continuous learning and improvement," she said. For Ornelas, the advantages of working for Pfizer include having the resources she needs to do her job, continuing growth opportunities and great benefits. "Yet what I like most about Pfizer," she says, "is that I continue to learn a great deal from my co-workers... Here, teamwork is taken seriously."

What excites her about working in the biomedical industry is the quest to find ways of improving the quality of life for people suffering from diseases like cancer. For young people with a similar passion, Ornelas recommends a biomedical career. She advises, "Aim high. Pursue a higher education. If you really want to be competitive, go to graduate school and get your Ph.D." That is advice that she says she will hold herself to and an ambition supported by Pfizer's continuing education program.

"Do what you love," she said. "You need to have the drive that comes from loving your every-day job."

Life Sciences Summer Institute

Students participating in hands-on lab experiments at the Life Sciences Summer Institute.

To excite students about science and pique their interest in a career in the life sciences industry, Life Sciences Summer Institute (LSSI) reaches out to both students and teachers through separate programs.

For the Student Internship Program, LSSI recruits upper-level high school, community college and university students and matches them with San Diego-based life sciences companies for a seven- to 10-week paid internship. The program enables young people studying science, math and engineering to explore career options, gain hands-on laboratory experience, practice work-readiness skills and secure mentoring by professional scientists and engineers. At the same time, participating companies or research institutions get a first look at prospective future employees while providing their employees with mentorship opportunities they might not otherwise have.

The student internship experience includes a week-long, pre-internship "Biotech Boot Camp" through the Southern California Biotechnology Center at Miramar College. There student interns learn key laboratory tasks, such as how to operate various pieces of lab equipment. They also polish their communication, organization, presentation and teamwork skills.

The LSSI student internship program has placed 173 students into hands-on industry internships, and 20 percent of the interns have continued to work part- or full-time for their sponsor companies.

Through teacher externships—the second program—LSSI seeks to energize local high school science teachers about the opportunities for their students in the life sciences industry. The Workforce Partnership estimates that each teacher reaches an average of 189 students every school year and can be a vital conduit for young people into a life sciences career.

To date, 70 teachers have completed the 12-day paid program. The program is hosted in Biogen Idec's Community Lab and includes training using the Amgen-Bruce Wallace Biotechnology Laboratory Program Curriculum. Teachers also complete half-day industry externships and half-day curriculum connection and implementation workshops.

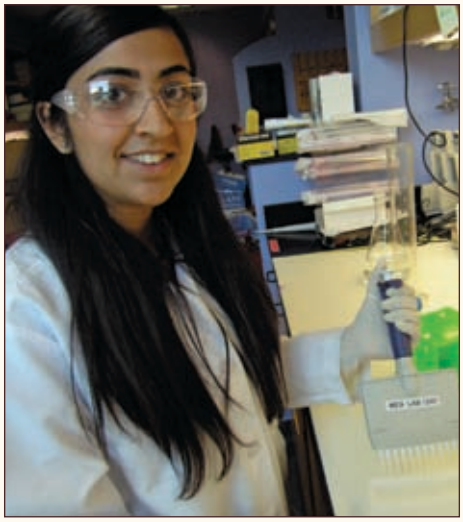
LSSI is a coordinated effort funded through its partners: San Diego Workforce Partnership Inc., BIOCOM, Amgen Foundation, Biogen Idec Foundation, Genentech, Gen-Probe, Invitrogen Corporation (now called Life Technologies), Pfizer Foundation, Southern California Biotechnology Center at Miramar College, California State University San Marcos, San Diego County Office of Education and the San Diego Science Alliance. In addition, student internships and teacher externships have been sponsored by more than 35 companies over the past four summers.

LSSI Student Profile—Aditi Sharma:

While pursuing a degree in Biomedical Engineering at the University of California San Diego, Aditi Sharma participated in the 2007 Life Sciences Summer Institute and was selected for an internship at Pfizer Global R&D La Jolla in the Cancer Biology/ Oncology Department. As an intern, she was able to gain hands-on laboratory experience and work with cutting-edge techniques and processes that are not taught in the classroom. She adapted and grasped concepts quickly and was a leader within her group. As a result of Sharma's hard work and outstanding performance, her supervisor asked her to continue as a part-time student laboratory assistant through the 2007 to 2008 school year and continue her work experience through summer 2008.

Also as part of the LSSI, Sharma was selected to work in a Nobel Prize winning laboratory with Dr. Stuart Lipton at Burnham Institute for Medical Research in stem cell research. This fall, Sharma was awarded a $3,500 scholarship by the Biotech Education Development Coalition, which will help her continue her goal to become a scientific researcher.

For more information on the LSSI program or to get involved, visit www.workforce.org or contact biotech@workforce.org.

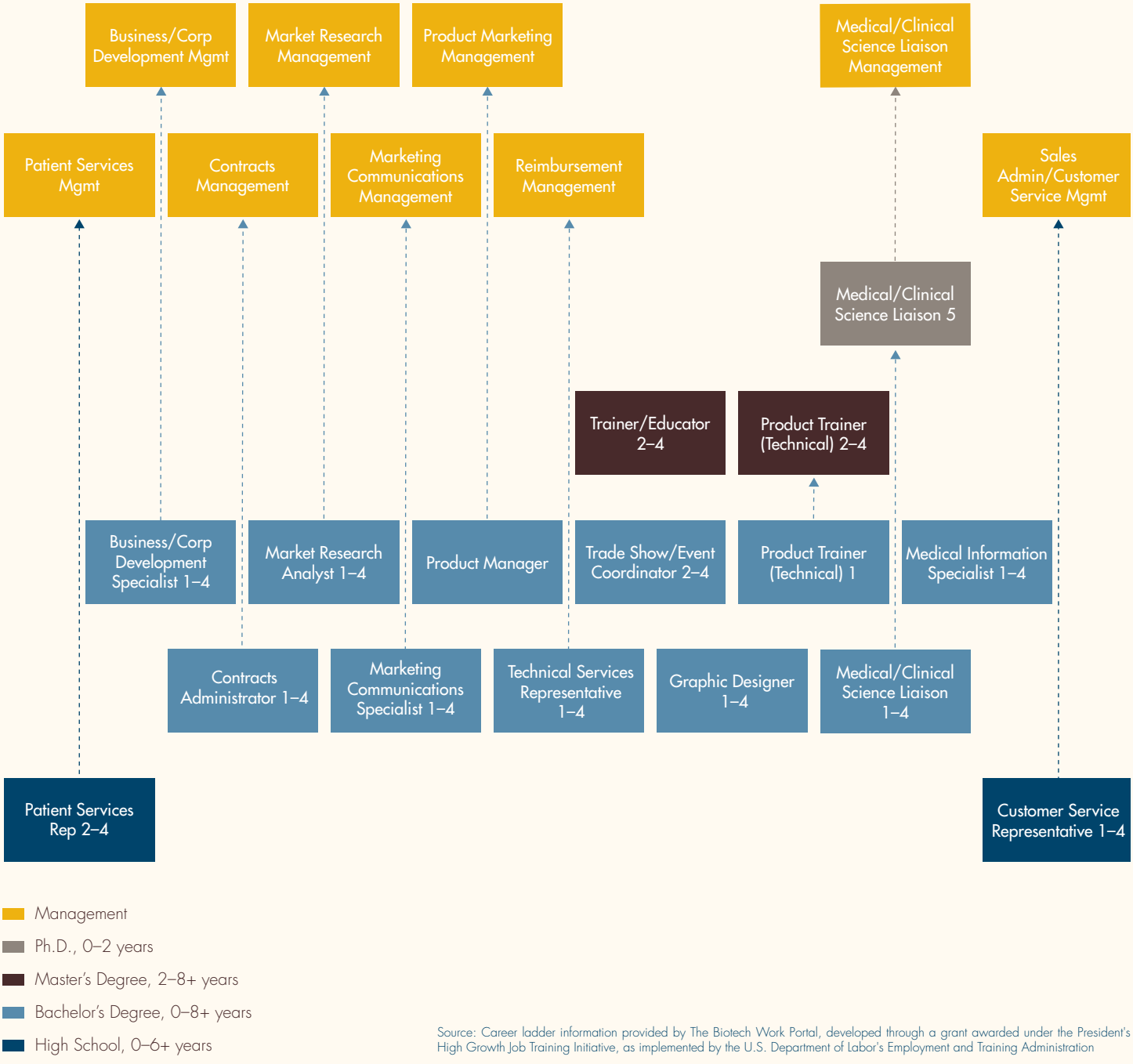


Aditi Sharma, LSSI participant

Biomedical Careers in California

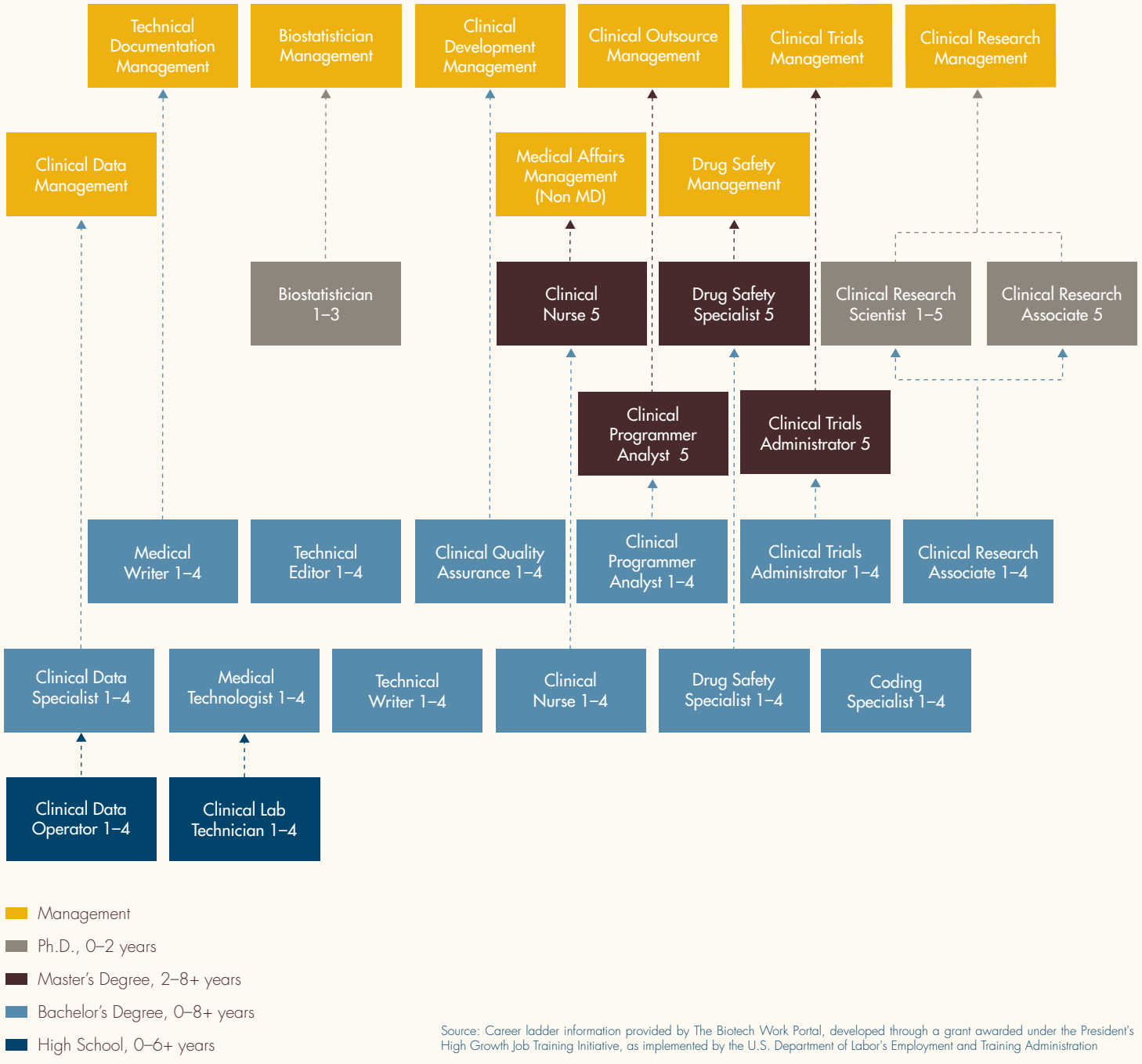
The biomedical industry is one of the fastest growing industries in California, offering excellent opportunities, pay and benefits to its employees with all levels of education, from high school diplomas to bachelor's, master's and doctorate degrees. Within each area of the biomedical industry there are many different job functions and within each job function are opportunities for entry-level jobs and often a career path. Occupational descriptions can fall into such sectors as research and development, manufacturing and production, quality control and quality assurance, sales and marketing, business and management and information systems. The following are just two examples of career ladders in the biomedical industry.

Figure 11: Business Development / Marketing / Sales Support Ladder Using Radford Job Titles



Source: Career ladder information provided by The Biotech Work Portal, developed through a grant awarded under the President's High Growth Job Training Initiative, as implemented by the U.S. Department of Labor's Employment and Training Administration

Figure 12: Clinical Ladder Using Radford Job Titles



Source: Career ladder information provided by The Biotech Work Portal, developed through a grant awarded under the President's High Growth Job Training Initiative, as implemented by the U.S. Department of Labor's Employment and Training Administration

Investment

Past editions of the California Biomedical Industry Report have featured Investment sections focused on the various transactions that fueled the life sciences sectors in the prior year. Traditionally, funding beyond product sales has come from venture capital, mergers and acquisitions and alliances. Those sources continued to drive the biomedical industry through 2007 and into 2008, and the following pages detail the commitment and support investors have provided California biomedical companies.

It would be disingenuous, however, to present that data and snapshot of the past as if business is continuing as usual. It is not. At press time, the global financial markets remain in a state of flux following the credit crisis of 2008. Investors are skittish. Funds, where available, are being held tightly until the economic landscape becomes more clear. Biomedical companies, once confident with two years of operating expenses in the bank, are growing increasingly anxious about their futures. From venture capitalists' board rooms to biomedical employees' kitchen tables, those whose livelihoods depend on the biomedical industry are discussing ways to cut expenses, stretch resources and optimize their returns on investment.

Just as the economy is dominating the new administration's agenda, it is upending the traditional maturation process—and, indeed, the life expectancy—of biomedical companies over the length of California. This issue of the California Biomedical Industry Report aims to put the past few years of financing activity into perspective as a way of benchmarking how devastating the unfolding situation may turn out to be.

Revenues

California's life sciences companies continued to expand through 2007. Total revenues from the state's biomedical sectors were $74.5 billion in 2007, an increase of 2 percent from the $72.8 billion reported in 2006.

The bulk of the industry's revenues were generated by publicly traded corporations, including homegrown giants such as Genentech, Amgen, Gilead and Allergan. The remaining firms predominantly are privately held, smaller companies with products still in development. In contrast to the profitable corporations, emerging and startup biomedical companies derive funding from individual investors, venture capital, debt vehicles and commercial contracts.

Venture Capital

Emerging biomedical companies have relied predominantly on venture capital to fund R&D until their products become "saleable," whether that means commercialized or out-licensed. In 2007, venture capital invested in California's life sciences (medical devices

and equipment as well as biotechnology) increased to $4.3 billion from $3.2 billion in 2006. The number of deals increased to 315 in 2007 from 299 in 2006. Biotechnology deals alone garnered $2.3 billion in 2007. That figure marks an increase of approximately 21.7 percent over the $1.9 billion raised in 2006.

In the first three quarters of 2008, California's biomedical companies completed 238 deals valued at $3.1 billion. That compared to 228 deals worth $3.2 billion in the same period of 2007. Biotechnology companies saw a marked decrease in investments, too. In the first nine months of 2008, biotechnology companies raised $1.6 billion, which compared to $1.7 billion in the same period of 2007. These decreases foreshadow the dwindling deal-making capabilities of biomedical companies in the coming quarters.

Comparing U.S. biotechnology investment in 2007 to that of 2006 reveals a shift in the company stage in development preferred by investors. Overall, investments increased 12.6 percent year-over-year while startup or seed financings fell 19.2 percent and funds for expansion stage companies decreased 17 percent. Early stage projects received $1.2 billion in 2007, an increase of 69.1 percent over 2006. Similarly, funding for later stage development companies in 2007 earned $2 billion, an increase of 34.5 percent over 2006's financings. These trends illustrate the preference that venture capitalist are displaying to fund companies that are further along the pathway toward drug development.

The California medical devices and equipment (med-tech) industry completed 151 deals in 2007 compared to 142 in 2006. The med-tech sector in California raised $2 billion in 2007, an increase of 47 percent over 2006's $1.3 billion. The first half of 2008 saw 88 deals valued at $1.1 billion.

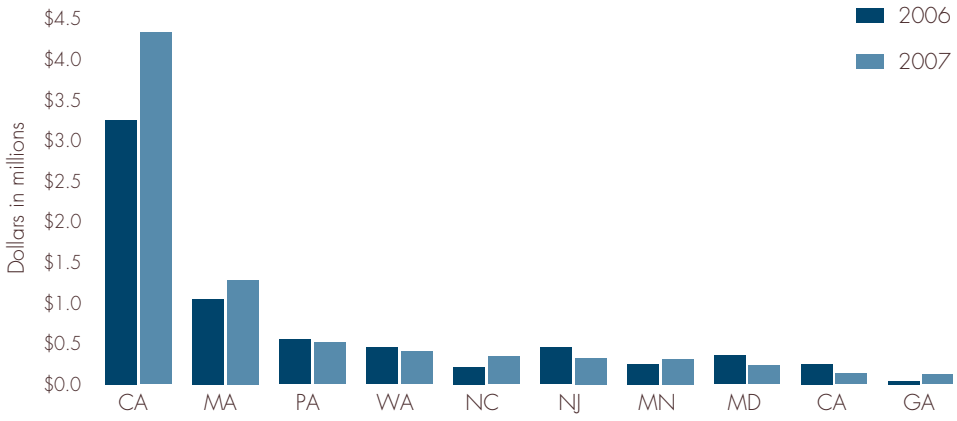
Figure 13: Venture capital investment in California life sciences companies first quarter 2006 to third quarter 2008, by sector

Quarter	Total	Biotechnology	Medical devices
Q1 2006	$755	$363	$392
Q2 2006	$717	$382	$335
Q3 2006	$793	$458	$335
Q4 2006	$969	$682	$287
Q1 2007	$1,392	$603	$789
Q2 2007	$1,007	$568	$439
Q3 2007	$802	$489	$313
Q4 2007	$1,082	$634	$448
Q1 2008	$1,050	$491	$559
Q2 2008	$1,002	$461	$541
Q3 2008	$1,014	$620	$394

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report, Data: Thomson Reuters

In 2007, California companies continued to draw more capital infusions than did life sciences companies in any other state. Total venture capital investment in U.S. companies in 2007 was $30.7 billion, an increase of 15.2 percent over the $27.0 billion in 2006. Of the 2007 amount, California companies were awarded $14.7 billion, or nearly 48 percent of the U.S. total. California's share in 2006 was 43 percent.

Figure 14: Venture capital investment in life sciences by state, 2006 to 2007 (dollars in millions)



Source: PricewaterhouseCoopers and National Venture Capital Association, Money Tree™ Report, 2007. Data from Thomson Financial

In 2007, venture capital investment in life sciences companies represented about 29 percent of total Californian venture capital investment, an increase from approximately 25 percent in 2006. For all industries in the state in 2007, venture capital investment totaled $14.8 billion via 1,630 deals.

Figure 15: Venture capital investment in California companies by year

Year	Companies	Deals	Investment ($M)
1997	921	1,129	6,029
1998	1,135	1,390	7,995
1999	1,745	2,204	23,132
2000	2,370	2,944	43,255
2001	1,296	1,527	16,6915
2002	930	1,070	9,4895
2003	941	1,125	8,558
2004	1,049	1,230	10,319
2005	1,128	1,306	10,958
2006	1,280	1,502	12,660
2007	1,343	3,931	14,769

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report, Data: Thomson Reuters

Initial Public Offerings

During 2007, 38 U.S. biotechnology companies issued IPOs and raised $13,922,461,792 in the process. That compared to 47 new U.S. biotech issues in 2006 and 44 in 2005. The most recent biotechnology IPO was completed by Nanosphere, an Illinois diagnostics company.[1] A number of biotechnology companies in the IPO queue publicly withdrew in fall 2008. Among them was Phenomix, a Costa Mesa, Calif. diabetes treatment company[2] and ChemoCentryx, a Mountain View-based developer of drugs for autoimmune, inflammatory and oncology diseases.[3]

Without question, the biotechnology IPO window is closed. Analysts predict that when it reopens, only a select few companies will be welcomed through. Those most likely to succeed will be companies with marketable therapies for indications such as hepatitis C, cancer and Alzheimer's disease.[4] Companies with late stage products, preferably those past their expensive clinical trials, will be most desirable.

Mergers and Acquisitions

Companies with marketable products—or at least late-stage development candidates—will continue to find success through mergers and acquisitions (M&A), too. Long a desirable exit strategy for medical technology innovators and their investors, M&A in recent years has enabled large pharmaceutical corporations to replenish their pipelines with start-up companies' technology platforms or lead compounds. Several noteworthy deals were completed in 2008. GlaxoSmithKline Plc acquired Genelabs Technologies of Redwood City for $57 million. That acquisition centered on Genelabs' therapies for the treatment of hepatitis C. Roche Holding AG, of Switzerland, continues to court Genentech in hopes of purchasing the GENE shares it does not already own.[5]

Yet not all M&A activity involves a bigger player gobbling up the smaller. In September 2008, Transcept Pharmaceuticals Inc. of Point Richmond and Novacea of South San Francisco announced their plans to merge. Privately held Transcept brings with it a late-stage development product for insomnia. Publicly traded Novacea, whose lead candidate failed in a late-stage cancer trial, offers nearly $100 million in cash. The combined entity will retain the Transcept name and, it hopes, will have the resources and product to become a profitable enterprise.[6]

Nuvelo, Inc. of San Carlos and ARCA Biopharma, Inc. in Colorado forged a similar merger in late summer 2008. That transaction is described in the profile of former Nuvelo chief executive officer and chairman, Ted W. Love, M.D., on page 13 of this report.

The med-tech industry also saw much more robust M&A activity in the 2005 to 2007 period than it did between 2002 and 2004. In fact, total M&A dollar volume was 3.5 times higher in the later period, according to Windhover Information, Inc. "Total deal dollar volume rose from $32 billion in the period 2002 to 2004 to more than $115 billion over the last three years," Windhover reported in April 2008. Because the number of deals remained flat at approximately 200 for each three-year period, the data show that med-tech deals have grown richer in recent years.[7] How the sector and its deal-making capacity fare in the current worsening recession remains to be seen.

Industry Alliances in California

Although large pharmaceutical corporations and the larger biotechnology companies seek

new products from emerging firms, their investments in earlier stage projects tend to be in the form of alliances rather than acquisitions. In 2008, California's biopharmaceutical, medical device and diagnostics companies benefited from research agreements and licensing deals with larger players.

As with the other avenues of financing discussed above, analysts anticipate that industry alliances will continue. The deal makers will be more selective, however, and will be better positioned to find bargains as the smaller companies face daunting economic realities.

The New Economic Landscape

The aggregate market capitalization of the 393 U.S. public biotech companies dropped from $350 billion to $344 billion in the first three quarters of 2008, according to the Biotechnology Industry Organization (BIO). As a whole, the companies worth less than $1 billion saw their aggregate value plummet by $13 billion to $40 billion. Shares in the industry leaders, including Genentech and Amgen, rose in the first three quarters. Similarly, the S&P 500 and NASDAQ composite indexes each dropped about 40 percent in the first nine months of 2008, whereas the Amex biotechnology index lost 22 percent and the NASDAQ biotech index fell 15 percent in the same period.[8] One reason for the relative resiliency of biomedical investments is that healthcare products are less vulnerable to downturns in the economy than other consumer products that can be delayed for flusher times.[9]

Support for healthcare products still in development is less reliable. In fact, for the first time, emerging biomedical companies are facing bankruptcy. In fall 2008, at least five biotechnology businesses sought bankruptcy protection, including Microlslet Inc., a San Diego developer of diabetes treatments, and Orchestra Therapeutics of Carlsbad, which was seeking a way to immunize patients against AIDS.[10] Others were thought to be headed toward a similar end.

Those at the highest risk of bankruptcy have experimental compounds moving into costly human research,[11] with no profit-generating products already on the market. The number of such companies is high. According to BIO, 38 percent of small biotechnology companies in the United States are operating with less than one year's supply of cash. Nearly 100 publicly traded biotech companies have less than six months' cash.[12]

With no access to the equity markets and little interest in licensing or development deals from pharmaceutical companies, startups with early stage products have no place to turn. Some are laying off staff and taking other cost-cutting measures. For example, Amylin Pharmaceuticals of San Diego, announced in November 2008 that it cut 16 percent of its workforce, or about 340 employees, in an attempt to save $80 million in 2009.[13]

To survive, other companies are narrowing their focus. In September 2008, Cytokinetics of South San Francisco announced it would jettison its cancer work to focus on a drug for

heart failure—and cut its workforce by 29 percent in the process.[14] Nektar Therapeutics of San Carlos recently sold its pulmonary technology platform to Novartis for $115 million in cash. The transaction allowed Nektar to retain and pursue its later stage products while off-loading technology it did not have the resources to develop further.[15]

Despite the promise of breakthrough new drugs, devices and diagnostics for pressing—and growing—unmet medical needs, emerging biomedical companies do not offer the same rates of returns that investors might find elsewhere. In fact, only seven of the 61 biotech companies to have gone public since 2000 are currently trading above their IPO prices.[16] Safety is outbidding rewards in the current financial markets.

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Investment:
Funding Startups in the Biomedical Industry

Guy Nohra
Co-founder and Managing Director
Alta Partners

Timothy Wollaeger
Managing Director
Sanderling Ventures

In a small courtyard within Genentech's South San Francisco campus is a life-size bronze sculpture commemorating the company's conception. It depicts venture capitalist Robert Swanson and biochemist and UCSF professor Herbert Boyer, PhD, in 1986 discussing an idea over drinks. Their idea, sketched on a cocktail napkin, would become Genentech, and their conversation spawned the biotechnology industry.

This famous meeting and ensuing collaboration also became the model of biotechnology and biopharmaceutical financings for the generation of entrepreneurs who followed. First, a scientist makes a breakthrough discovery (in this case, recombinant DNA). He or she teams up with an investor to move the idea through proof-of-concept and into clinical trials. As the company progresses—and its funding needs grow—it completes a lucrative initial public offering (IPO) that repays the investors, rewards the founders and enables investors to participate in the company's increasing value.

Iconic though this storyline for biomedical industry success may be, today's venture capitalists explain that building successful companies is neither simple nor certain. "For every Genentech from that vintage," said Guy Nohra, co-founder and managing director of Alta Partners in San Francisco, "there were 15 companies that did not succeed," a ratio that continues today.

Nor has the playing field remained the same. "The bar keeps getting higher," Nohra said. "Today to go public, a company must have positive Phase II data. Getting to that milestone means a lot more money has to be raised through equity" than was required in the late '80s and early '90s.

Timothy Wollaeger, managing director of Sanderling Ventures and the founder of several life sciences companies, said, "Every company I have been involved in has had significant mid-course corrections. No one ever gets through the first five years and says, 'We did exactly what we said we'd do.'" Neither the business nor the business model is simple.

While the classic model of success for biotech investors has been an IPO, medical device startups have frequently created liquidity for their investors through acquisitions by larger companies.

Given that there is no guaranteed pathway or sure route to recouping investment dollars, venture capitalists look for solid fundamentals in their companies. "We are essentially in the business of backing people," Nohra said. "We look for entrepreneurs who are very intelligent. They need to have an entrepreneurial vision and be good leaders. Previous experience is also helpful, but not necessary if the other attributes are there."

"The company has to be targeting a viable market with significant unmet needs," said William J. "Bill" Link, Ph.D., co-founder and managing director of Versant Ventures in Newport Beach. "We look for something special from a technology standpoint. The

product must be a breakthrough that does something new, does something better or does something less expensively."

Assured by the inventor's team and a strong potential market, the venture capitalist calculates the resources—money, time, personnel and facilities—it will take to commercialize the idea. The investor determines whether he can raise those resources and his probability of realizing a return on the investment in the future.

"Everything we do takes more money and takes a longer time than it used to," Nohra, who specializes in med-tech investments, said. "The FDA is a little slower. Our companies face a lot of competition. Reimbursement is a big issue, especially for new technologies."

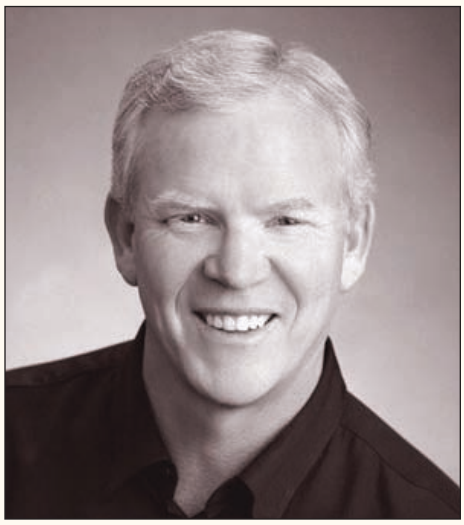
The financial markets, too, are critical to the ability to raise investment capital. "The current financing environment is confusing," Link said. "This is not a good time in the financial markets, and we don't know how deep and long-standing [the current financial crisis] will be." He said he is not worried about the future of the biomedical innovators. "People need healthcare. There is a continuous demand for important healthcare products that keeps the industry largely buffered from troubles in the financial markets." He added, "We hope to keep companies financed and believe that we can still create value."

For biopharmaceutical and med-tech innovators alike, the venture capitalists had sage advice. "Yes, live your dream," Nohra said. "But surround yourself with people who know what they are doing. Find a lawyer who understands the biomedical industry and its intellectual property and patent protection concerns." He added that selecting venture capitalists who specialize in the biomedical industry is critical—and that the investors can recommend experts to fill out the innovator's team.

Link cautioned would-be entrepreneurs to take a step back from the bench. "Researchers working on a project tend to be passionate about their work. They need to be passionate about it," he said, "but they also need to be objective and ask, 'How many people could this help?'" If their answer spotlights a significant market with an unmet medical need, chances are they can find the resources they need in California to commercialize their product.

"I can't describe any place that's better" than California for biomedical startups, Wollaeger said. "There are many entrepreneurs here. There are educated people here. We have the facilities and resources to support science. We have the requisite specialists, both in medical technologies and in business. And there are lots of VCs here."

Genentech and the biotechnology industry were not the only offspring of the Swanson/Boyer collaboration. The life sciences venture capitalist model was conceived with them, too. And nothing attracts investment capital or inspires inventiveness like those 1-in-15 success stories.



William "Bill" J. Link, Ph.D.
Co-founder and Managing Director
Versant Ventures

PROFILE

Shiva Malek, Ph.D.

Shiva Malek, Ph.D, is a scientist in biochemical pharmacology at Genentech in South San Francisco. She pursued her education through the University of California system, earning her bachelor's degree in biochemistry from UCLA, her master's in chemistry at UCI and her doctorate in biochemistry from UCSD. Malek worked for smaller biotechnology companies, including Vertex Pharmaceuticals and Exelixis, before joining Genentech in 2006.

Shiva Malek, Ph.D., joined Genentech to help build the company's growing small molecule drug discovery group. Unlike large-molecule human proteins produced by genetic engineering, which typically need to be injected, small molecules are chemical compounds that can be taken as pills. She currently manages a staff of seven scientists and research associates in the biochemical pharmacology department, a group that develops and validates enzyme and cellular assays to support small molecule drug discovery projects. They also work closely with other scientists in the early leads, medicinal chemistry, protein engineering and oncology research groups to support projects from high-throughput screening, lead validation, lead optimization, through candidate selection. Malek also serves as the project team leader for one of Genentech's late-stage research oncology programs.

"We have a really fun, dynamic environment at Genentech," Malek said. "There is extensive collaboration among departments. I work with many gifted scientists who are scientifically engaged and eager to understand the perspectives of the other disciplines represented on the teams." She added, "Genentech hires the very best and enables project teams to make the right decisions based on high-quality data."

Malek focuses on small-molecule oncology products and says she finds great personal satisfaction in working to advance therapies in areas like cancer where present treatments are inadequate. "I truly believe that our work is doing good for patients and their families." She added, "Most of us who work in biotech really take our work personally. Helping patients and expanding science and medical knowledge are big components of why people pursue careers in the biomedical industry."

She would encourage young people to seriously consider a future in life sciences. "Really explore," she said, "and find the area in science that you feel passionately about. If you are passionate about your research, graduate school is the most fun you will ever have." She noted that a science background opens up a wide range of career paths in academia, research and industry.

"This is an exciting time," she said. "The work we are doing improves healthcare, and the demand for that isn't going to go away. Additionally, as we learn more about disease processes, our strategies around developing therapeutics to either modify disease course or even cure a disease will expand. In parallel, utilizing newer and more effective technology platforms to enable drug discovery is an important component of our work as we continue to be at the forefront of drug discovery."

While Malek cannot predict the future for the biomedical industry in California, she noted that she and her husband, a physician, settled in the Bay Area for the opportunities the region offers for both. "I'm here specifically because I think it's a great place to be."

Angus Sinclair, Ph.D.

PROFILE

Angus Sinclair, Ph.D., is a principal scientist in the hematology research department at Amgen's Thousand Oaks campus. He earned his bachelor's degree in molecular biology from The University of Edinburgh in Edinburgh, Scotland and his doctorate in hematology from the National Institute for Medical Research/University College in London. After conducting post-doctoral research for eight years in labs at the University of California San Diego, University of Cambridge in the U.K. and the University of Texas at Dallas, he joined Amgen in 2002.

At Amgen, Angus Sinclair, Ph.D., leads a group of eight scientists—five in Thousand Oaks and three in Cambridge, Mass. Their department plays two key roles: drug development and drug support. The first is to support discovery research by identifying molecular targets and therapeutic molecules that might cure or treat hematology (blood) and oncology (cancer) diseases. Their work spans the development process from discovery to clinical testing.

The department's second key function serves Amgen later in the drug development process. The team endeavors to further understand the products' mechanisms of action, that is, how they work at cellular and sub-cellular levels, and to further understand the basic biology of disease and help identify potential new indications. Such knowledge helps inform discovery and development decisions for future compounds and may clarify therapeutic parameters for existing products.

Sinclair said he has been impressed with the integrity of the science and with the resources available to him in Amgen's labs. He especially enjoys the multifunctional teams with which he works. "In conducting basic research in academia," he said, "you're often working as a sole scientist on projects that you hope would one day benefit patients and would help others better understand disease…Here, we are doing groundbreaking research that leads to products that are helping real people in real time. And I'm working with teams of highly motivated and qualified people."

Sinclair added that the staff at Amgen is diverse and accepting of individual differences. "Amgen expects a high level of performance, and that requires leveraging everyone's unique perspective and experience." He said that intra-team trust includes relying on one another's professional expertise and respecting cultural and personal differences. He noted that he is gay, and "at Amgen that is such a non-issue."

As a company, Amgen has actively encouraged a "culture of inclusion." The company sponsors more than 28 affinity group chapters at multiple sites that provide mentoring and networking opportunities as a part of Amgen's goal to engage, develop and retain staff. More than 2,500 staff members participate in such affinity groups as the Amgen Asian Association, the Amgen Black Employees Network, the Amgen Latin Employees Network, the Amgen Women's Interactive Network, and the Amgen Network for Gay and Lesbian Employees, for which Sinclair currently serves as chair.

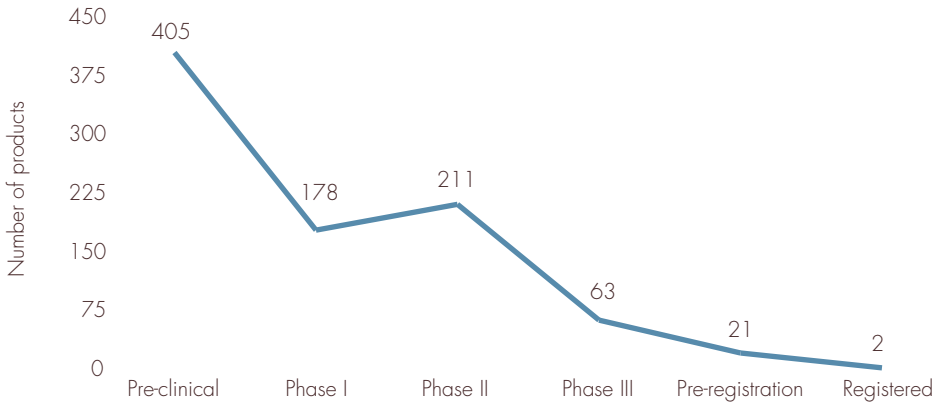
"I would absolutely recommend pursuing science and a biomedical career," Sinclair said. He would advise young people—or adults looking to change careers—to network and talk with others about working in a biomedical setting. Many companies, including Amgen, have internship, mentorship and post-doctoral opportunities that enable students or recent grads to see firsthand what it is like to work in industry. Sinclair added, "Research really isn't the only opportunity." Beyond science, biomedical companies need business, legal, communications, IT, sales, manufacturing and many other types of professionals.

Product Development: California's Biopharmaceutical Pipeline

Murray L. Aitken is senior vice president, Healthcare Insight, responsible for leading IMS's thought leadership initiatives worldwide. He joined IMS in July 2001 and was initially responsible for the growth and development of the company's consulting and services businesses. Named to his current role in August 2007, Aitken previously was senior vice president, Corporate Strategy. Aitken received an M.B.A. degree with distinction from Harvard University in 1987. He also holds a Master of Commerce degree from the University of Auckland in New Zealand.

Global sales of biotechnology and pharmaceutical products reached $663 billion in 2007, representing growth of 6.1 percent over the prior year. Of that total, $75 billion of sales were of biotech products, which saw a healthier annual growth of 12.5 percent. At the end of June 2008, there were almost 900 products in the pharmaceutical pipeline (including those in pre-clinical testing, clinical development and in the process of registration) that were originated by, or invested in, by California companies. The California pipeline represents 15 percent of the global biopharmaceutical pipeline of 5,828 products.

Figure 16: Number of biopharmaceuticals in California product pipeline



Source: IMS Health R&D Focus July 2008

Since January 1, 2007, four of the 28 new chemical or biological products launched in the United States had connections to California companies. For example, in June of 2007, Letairis (ambrisentan), a selective endothelin receptor antagonist (ETA), was launched in the U.S. by Gilead Sciences in Foster City, Calif. for the treatment of pulmonary arterial hypertension. This represents an advance in therapy as this is the first selective ETA on the market.

In another example, Kuvan (sapropterin) was launched in the U.S. in December 2007 by BioMarin. Kuvan is used as a therapy for phenylketonuria (PKU), a genetic disorder that is characterized by an inability of the body to utilize the essential amino acid, phenylalanine. In infants and children, this can result in mental retardation, smaller brain size, delayed speech and other neurologic problems. About one in 12,000 to 15,000 infants in the U.S. is born with PKU. Both Letairis and Kuvan have received Orphan Drug designation by the FDA, which reflects the novelty of the therapies and their focus on diseases affecting fewer than 200,000 people. These products are expected to bring

significant benefits to those patients suffering from the conditions described.

The FDA has also granted Cephalon's Treanda (bendamustine) Orphan Drug status for the treatment of chronic lymphocytic leukemia (CLL), a type of leukemia, or cancer of the white blood cells. Still in the pipeline, Avencia's Phase III drug ALS-02 was granted Orphan status for the potential treatment of amyotrophic lateral sclerosis (ALS) in March of 2002, and Inotek and Genentech have a development deal for INO 1001 a Phase II product, which was granted status in February of this year to prevent postoperative complications of aortic aneurysm repair.

Oncology

California continues to produce significant numbers of products in active preclinical testing or clinical development. Of the total 880 product candidates, 452 (51 percent) are being evaluated in clinical trials. The top six disease foci comprise 89 percent of the California biopharmaceutical pipeline with oncology being the largest area of focus with 282 products. Amgen and Genentech, both headquartered in California, have numerous pipeline products in this area. For example, Amgen is developing denosumab (AMG 162), a potential treatment for postmenopausal osteoporosis, cancer treatment-induced bone loss (TIBL) in prostate or breast cancer patients, giant cell tumor of bone, bone loss in patients with metastatic bone disease and rheumatoid arthritis. Denosumab is in Phase III for osteoporosis and appears to have the potential to be a blockbuster drug, with peak sales globally in excess of $1 billion. Genentech and Seattle Genetics are in Phase II development of dacetuzumab (SGN 40), a humanized monoclonal antibody for the treatment of hematological malignancies. It has been granted Orphan Drug status specifically for the treatment of multiple myeloma and chronic lymphocytic leukemia.

Central Nervous System

The number of clinical products in the pipeline for therapies addressing the central nervous system (CNS) was 131. These products make up more than 14 percent of California's pipeline with leading manufacturers such as

Figure 17: Top disease foci in California's product pipeline

Disease Focus	Number in CA pipeline
Oncologics	282
Central Nervous System	131
Infectious Diseases	115
Immune System and Inflammation	92
Cardiovascular and Blood Diseases	88
Diabetes and Metabolics	79

Source: IMS Health R&D Focus July 2008

TorreyPines Therapeutics of La Jolla, Calif. and Acadia in San Diego. TorreyPines is in Phase II development of tezampanel, as a potential treatment for migraine and pain. So far, in all testing, all doses have been well tolerated with no serious adverse events reported. Acadia is in Phase III development of pimavanserin as a therapy for treatment-induced dysfunctions in Parkinson's disease. Pimavanserin is also being investigated as a potential antipsychotic agent with improved side effect profiles, and as a treatment for anxiety and sleep disturbances.

Infectious Disease

California's infectious disease pipeline includes 115 products, about 13 percent of the pipeline. Cerexa located in Alameda, Calif. has exclusive license to develop and commercialize Phase I drug, ME 1036, an injectable carbapenem for the potential treatment of severe systemic bacterial infections. ME 1036 is being developed for the treatment of hospital acquired infections, including pneumonia, complicated skin and skin structure infections, complicated intra-abdominal infections, urinary tract infections and bacteremia. Another example of a novel product being developed in California is oritavancin, a novel semi-synthetic glycopeptide antibiotic being developed for the treatment of serious Gram-positive infections. Originally discovered and developed by Eli Lilly, it was licensed by InterMune and then by Targanta Therapeutics.

Immunological and Inflammatory Disorders

Products in development in the broad range immunological and inflammatory disorders include 92 California products. Companies like Ligand Pharmaceuticals in San Diego and Amgen in Thousand Oaks, Calif. make strides to bring innovative products to the market in this area. Atlantic Healthcare is currently in Phase III development of alicaforsen, for the treatment of ulcerative colitis (a form of inflammatory bowel disease), Crohn's disease (an inflammatory disease of the digestive system), psoriasis (a non-contagious disorder which affects the skin and joints) and is also being investigated for the treatment of pouchitis, an inflammatory bowel disease. The FDA has granted this novel therapy Orphan Drug designation for the treatment of pouchitis. The original patent holder Isis, of Carlsbad, Calif., signed an agreement with Atlantic Healthcare granting them worldwide exclusive rights to alicaforsen and second generation ICAM-1 antisense compounds. This constitutes 10 percent of the California pipeline and includes products for indications such as pain, rheumatoid arthritis, psoriasis, asthma and ulcerative colitis.

Cardiovascular Disease

The fifth largest focus of the California drug pipeline is cardiovascular disease, with approximately 88 programs in the pipeline. This is about 10 percent of the overall pipeline. Cardium Therapeutics is developing alferminogene tadenovec (GENERX), a gene therapy for angina associated with coronary artery disease. The therapy is delivered by intracoronary injection, a minimally invasive approach that the company expects may provide an alternative to angioplasty and coronary artery bypass graft surgery. Presently alferminogene tadenovec is in Phase III trials, but they have been granted Fast Track status by the FDA for the treatment of myocardial ischemia. GlaxoSmithKline's Promacta (eltrombopag), an oral non-peptide platelet growth factor that mimics the activity of thrombopoietin, is being developed as a potential therapy for thrombocytopenia, the presence of relatively few platelets in blood, caused by chemotherapy or radiotherapy, as well as for the treatment of anemia and neutropenia in cancer patients. The product is currently in pre-registration and the FDA has granted it Priority Review status for the treatment of chronic short-term idiopathic thrombocytopenic purpura (ITP), a condition of having a low platelet count (thrombocytopenia) of no known cause.

Diabetes and other Metabolic Disorders

Medicines for diabetes and other metabolic disorders make up about 9 percent of California's biopharmaceutical pipeline, while interest is still growing in this category. Akesis is in Phase II development of AKP 020 for potential use in the oral treatment of type 2 diabetes. AKP 020 may be used as a monotherapy or in combination with other diabetes treatments. Safety, efficacy and pharmacokinetics studies of the product in patients with type 2 diabetes began in November of 2007. Metabolex in Hayward, Calif. and Ortho-McNeil are developing the oral compound metaglidasen, also as a potential therapy for type 2 diabetes. The agent also lowers triglycerides and low density lipoprotein while increasing high density lipoprotein levels.

2008 FDA Approvals/Clearances

- Abbott: First fully automated blood screening test for HTLV-I/HTLV-II
- Abbott: SIMCOR (Niaspan/simvastatin), a novel combination medicine for comprehensive cholesterol management
- Abbott: HUMIRA (Adalimumab) the first biologic treatment approved in nine years for children suffering from this potentially debilitating autoimmune disease
- Abbott: FreeStyle Navigator for proactive diabetes management
- Abbott: ARCHITECT i1000SR Analyzer
- Abbott: XIENCE V drug eluting stent
- Allergan: Trivaris (triamcinolone acetonide injectable suspension) eye infection drug
- Amgen: Nplate for the treatment of adult chronic immune thrombocytopenic purpura
- Bayer: Contrast agent Primovist for the detection and characterization of liver lesions
- Baxter: Artiss, a sealant used in adhering skin grafts to burn patients
- BD Diagnostics: GeneOhm StaphSR test to identify two fatal healthcare-associated infections from patients with positive blood cultures
- Eli Lilly & Co.: Cymbalta for the management of fibromyalgia
- Eli Lilly & Co.: ADHD drug Strattera, the first FDA-approved non-stimulant to treat ADHD in children, adolescents and adults
- Genentech: Avastin to treat breast cancer
- Gilead: Chronic hepatitis B treatment Viread, also indicated for HIV infection in adults
- Johnson & Johnson: OneTouch Ping insulin pump
- Life Technologies: SPOT-Light HER2 CISH Kit, an aid in the assessment of breast cancer patients for whom trastuzumab (Herceptin) treatment is being considered.
- Medtronic, Inc: OneTouch UltraLink Meter certified to wirelessly communicate with Medtronic diabetes management products
- Medtronic: Talent thoracic stent graft as a minimally invasive treatment for certain types of aneurysms of the descending thoracic aorta
- Medtronic: Endeavor, first new drug-coated stent in four years
- Medtronic: New neurostimulator with patient programmer
- Medtronic: Attain StarFix, the first-ever active fixation left-heart lead for cardiac resynchronization therapy
- Merck & Co.: EMEND (fosaprepitant dimeglumine) for injection, a new intravenous therapy for the prevention of chemotherapy-induced nausea and vomiting (CINV)
- Novartis: Tekturna HCT as a single-tablet combination of two high blood pressure medicines—Tekturna and the diuretic hydrochlorothiazide
- Novartis: Single pill combinations diovan HCT and Exforge approved as first-line treatments for high blood pressure
- Thermo Fisher: MRSA test to screen for methicillin-resistant Staphylococcus aureus, more commonly known as the 'superbug'
- Wyeth: Pristiq (desvenlafaxine succinate) antidepressant

Product Development: The Future of Ophthalmic Innovations

David E.I. Pyott
Chairman and CEO
Allergan

James V. Mazzo
Chairman and CEO Advanced Medical Optics, Inc. (AMO)

In the course of a lifetime, humans experience a number of ophthalmic, or eye, disorders. From needing corrective lenses to requiring cataract surgery, each of us, at different ages, faces the risk of eye disease.

Among the most debilitating ophthalmic conditions are glaucoma, macular degeneration, diabetic retinopathy, dry-eye syndrome, infection and inflammation. Many of these are age related and their incidence and prevalence are increasing as people live longer. Several are co-morbidities of diabetes and other chronic diseases that also are increasing in the United States and California.

As anyone who has ever had an insect fly into her eye knows, conditions that affect one's vision or cause discomfort in eyes are quite debilitating. Studies have quantified the effects of chronic ophthalmic conditions on productivity. One recent study out of Johns Hopkins showed that chronic ophthalmic conditions and low visual acuity are reliable predictors of lost work hours and significantly lowered productivity.[1] Individuals with these conditions also are less likely to seek employment, given their limitations.

Innovations in the Golden State

Recent California-spawned innovations in the treatment of ophthalmic disorders are delivering marked benefits to patients while reducing the economic and social burden of the conditions. Such progress has improved pharmaceuticals, surgical procedures, ophthalmic implants and reimbursement practices.

Pharmaceuticals: Allergan, Inc. is the world's second largest and fastest growing ophthalmic care company for the past six years, with headquarters in Orange County since 1971. The company's robust product offerings have long included therapies that offer relief to dry eye sufferers, lower intraocular eye pressure in patients with glaucoma, and reduce symptoms of external eye diseases.

More recently, Allergan embarked on its debut into the retina market with the FDA approval of Trivaris, a corticosteroid approved for ophthalmic use. Later in 2008, the company intends to file a new drug application to obtain market authorization for Posurdex, a novel drug delivery system that will deliver compounds directly to the back of the eye and is currently being investigated to treat macular edema associated with retinal vein occlusion. Not only does Allergan believe that the device, if approved, will provide more effective results, but will help reduce the side effects commonly associated with systemic medications currently available to patients.

Allergan is committed to quality products that are meaningful to patients and represent true scientific advancements in eye care, as exemplified by its dry eye treatment portfolio. When the company began developing its latest product in this area, the challenge was two-fold: researchers had to show that the product was safe and efficacious in a disease that had not been previously defined.

"Dry eye is an inflammatory disease that, over time, destroys the cells in the cornea," said David E.I. Pyott, chairman and chief executive officer of Allergan. "It was very complex

to prove the mechanism of action for Restasis," he said, but the company was able to show that the prescription eye drop helps increase the eyes' natural ability to produce tears. Pyott added that the eye drop, which obtained FDA approval in 2002, is the only prescription dry-eye product in the world. He expects it will generate approximately $450 million in worldwide sales in 2008.

Looking ahead, Allergan's ophthalmic pipeline is focused on back-of-the-eye diseases such as macular edema, diabetic retinopathy and age-related macular degeneration. "These diseases cause sight loss in thousands of patients each year," Pyott said, "and their prevalence is increasing as the population ages. The potential approval of Posurdex will certainly help address a high unmet need." Continuing its interest in glaucoma treatments, Allergan also is investigating the next generation of drugs to lower intra-ocular pressure as well as ways to harness ocular implant technology to deliver compounds to the back of the eye in order to protect cells against glaucoma.

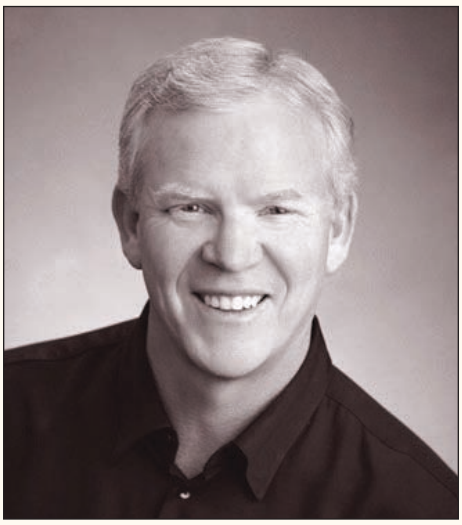
Surgical devices: Until six years ago, Allergan owned an ophthalmic surgical device division that today commercializes lasers, blades and intraocular lens implants for use in cataract and other eye surgeries. "Allergan's senior management evaluated the overall company, and recognized that we were running two fundamentally different businesses," said James V. "Jim" Mazzo, formerly Allergan's corporate vice president and president of the ophthalmic surgical and contact lens care businesses.

"We had the pharmaceutical business and we had medical devices. Because the businesses marketed in different ways to different customers on different product lifecycles and at different margins, we realized we couldn't operate both [divisions] to their best potential." In July 2002, Allergan spun off the surgical device unit, Advanced Medical Optics (AMO), with Mazzo as chairman and chief executive officer.

The separation enabled AMO to focus entirely on the ophthalmic device sector. "Our goal was to increase both the breadth and depth of our offerings to ophthalmologists and optometrists," Mazzo said. Because technology continues to change so dynamically in its sector, AMO has accomplished that goal several times over. The company's latest surgical technology introduction is Healon D viscoelastic, a viscosurgical device used in cataract extraction, intraocular lens implantation, corneal transplants and glaucoma filtration surgery. The low molecular weight Healon D coats the cornea and remains in place throughout the surgical process to provide lubrication of intraocular lense insertion systems.

The company also branched out, making acquisitions to broaden its pipeline and to gain traction in related sectors. AMO purchased Pfizer's surgical ophthalmology business in 2004 and, with it, key lines of viscoelastic products used in ocular surgery, intraocular lenses and a glaucoma shunt. It also acquired two leading LASIK surgery technique and technology providers, VISX of Santa Clara, Calif. in May 2005, IntraLase Corporation of Irvine in April 2007 and WaveFront Sciences, Inc. of Albuquerque, N.M. in January 2007.

As surgical and other therapeutic techniques improve, they can alter the entire field. That



William "Bill" J. Link, Ph.D.
Co-founder and Managing Director
Versant Ventures

Michael V. Drake, M.D.
Chancellor
University of California, Irvine

is what is happening with LASIK surgery, which works by changing the shape of the eye itself. As the first wave of LASIK recipients begins to require cataract surgery, surgeons must change their calculations for the altered eye shapes. WaveTec Vision Systems in Aliso Viejo, Calif. is addressing that new and unexpected consequence. The startup company is developing an instrument that attaches to the surgical microscope to enable the physician to more precisely measure the patient's corrected vision.

Ophthalmic implants: Another Orange County eye device company, Glaukos Corporation, is approaching glaucoma from a non-pharmaceutical angle and one designed to improve upon the invasive surgical techniques currently employed. The company has developed a minute titanium stent that can be implanted in the eye to drain fluid and thus reduce the pressure that leads to glaucoma.

Premium lenses: Every year, the most common ophthalmic surgery performed is cataract removal. Nearly 3 million such surgeries are performed annually, and each year, a greater percentage of the patients are Baby Boomers, who are more reluctant than earlier generations to wear eyeglasses.

Eyeonics responded with a premium lens that not only replaced the cataract but provided vision correction to enable patients to read without glasses or contacts. Eyeonics reported $34 million in revenue for its premium lenses in 2007, and in February 2008 was purchased by Bausch & Lomb.

Orange County and Ophthalmic Innovation

Bausch & Lomb not only obtained new products in its purchase of Eyeonics; it obtained a toehold in Orange County, which has been called the epicenter of ophthalmology innovation.

Thanks to spin-offs from Allergan and start-ups founded by former Allergan, AMO, Chiron Vision and others' employees, Orange County currently boasts several dozen biomedical firms that are developing intraocular lenses, laser surgery instruments and mechanical and pharmaceutical treatments for glaucoma and other eye diseases. Innovators who successfully built and sold businesses have gone on to form additional new biomedical or biomedical-related firms.

Among this latter group is William J. "Bill" Link, Ph.D., co-founder and managing director of Versant Ventures, who earned his engineering doctorate from Purdue University and moved to Orange County in 1977 to work for a hospital supply company. When he learned of a need for intraocular lenses in cataract surgery, he founded American Medical Optics. That company—the predecessor of Advanced Medical Optics—was sold to Allergan in 1986. Link then founded Chiron Vision, as an Orange County eye-care subsidiary of Chiron Corporation. After selling Chiron Vision to Bausch & Lomb in 1997, Link became a venture capitalist at Brentwood Venture Partners and its successor firm, Versant Ventures. As an investor, he has helped to fund 20 companies, half of them in Orange County.

UC Irvine Fueling Scientific Innovation

Yet commercial success and financial resources are not all that Orange County has to offer. University of California, Irvine sits in the heart of the county and has long contributed to the scientific knowledge in the ophthalmology field. In fact, with the help of the companies mentioned above, UCI soon will be home to a new, $55-million eye institute to be named for Gavin S. Herbert, Allergan's founder and former chairman.

The center, said Michael V. Drake, M.D., UCI's chancellor, will consolidate research and clinical care in a state-of-the-art facility. Several years of planning have gone into the project, and the bulk of the financing will come from private sources. "We have identified and set aside a site on campus for the facility, and the planning committee is settling in on the programmatic aspirations for the center. We are very committed to the project and could begin construction in a year or two."

Among the planning committee's goals for the eye institute is that it become the best ophthalmology institution in the United States. As such, it will pursue education, research, patient care, clinical testing and technology transfer activities. And it will expand the university's influence and involvement in the local biomedical community.

"There always has been flow to and from UCI and the local companies," Pyott said. He pointed to temporary assignments of Allergan employees on campus and UCI faculty and post docs at Allergan. The university is a rich source of interns and outside expertise, and Allergan employs more than 200 UCI science and business graduates.

For Mazzo, the eye institute is a personal passion. Gavin Herbert was his mentor and friend, and naming a world class eye institute in Irvine after him is a fitting tribute. AMO works with the leading eye institutes around the world, and will continue to do so, Mazzo said. Yet the Gavin S. Herbert Eye Institute would add so much to the local biomedical community, he said.

"Being within proximity of the pioneers of our sector helps," Mazzo said. "It's good to be able to share thoughts and ideas, to inspire one another with direction and knowledge. And having all of these resources in one area gives us confidence in our own dreams and future success."

Having seen others' success, ophthalmology-focused innovators envision a bright future for their ideas and companies in Orange County.

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1. Source: Jacobson G, Frick K, Massof R. Impact of Low Vision and Chronic Ophthalmic Conditions on Absenteeism and Lost Work Productivity. *Abstr AcademyHealth Meeting*, Boston, Mass., 2005; 22: abstract no. 4117.

A Silent Menace: Chronic Hepatitis B in California's Asian-American Community

Fiona Ma is the California assemblywoman representing San Francisco and San Mateo counties and, as assembly majority whip, the highest ranking Asian-American woman in the state legislature. Elected to the Assembly in 2006, Ma has championed programs to protect children from toxic chemicals, grow California's economy and bring high speed rail to the state. She has also been a vocal advocate for screening, vaccinating and treating California's Asian-American and Pacific Islander populations for hepatitis B virus, a chronic and potentially debilitating illness that Ma contracted at birth. Prior to being elected to the state assembly, Ma served as an aide to John Burton, an assemblyman and congressman who was leader of the California State Senate. She also was elected to the San Francisco Board of Supervisors in 2002. Ma earned her Bachelor of Arts degree from Rochester Institute of Technology, her master's degree in taxation from Golden Gate University, and her MBA from Pepperdine University. She resides in San Francisco's Sunset district.

When Fiona Ma was 22, she volunteered to donate blood at her company's blood drive. Following routine screening, however, she was turned away: her blood tested positive for the hepatitis B virus (HBV).

"I asked my mother," after the blood bank incident, "and she said that, yes, I had it." Ma, like many of those with hepatitis B, had contracted the disease from her mother in childbirth. "She said not to worry, though, because I was only a carrier." Ma was assured that carrying the disease was not the same as having it.

A few years later, Ma participated in a press conference with Samuel So, M.D., the director of the Asian Liver Center at Stanford. "I was asked to speak because I was an Asian American with hepatitis B." She repeated what her mother had told her about having nothing to worry about. "After the event, So said to me, 'Young woman,…?'" He made it clear to her that she needed to take better care of herself and to monitor her health more closely.

What So told her was frightening. Chronic HBV is a serious and potentially fatal liver disease. Chronic HBV can slowly destroy the liver, causing scarring (cirrhosis), chronic liver disease or primary liver cancer. Believed to cause 80 percent of all liver cancer cases worldwide, HBV is second only to tobacco among known human carcinogens.

So and Ma's own research revealed that the impact of chronic HBV in the United States is heaviest among Asian Americans and Pacific Islanders. An estimated one in 10 foreign-born Asian Americans is living with chronic HBV infection, compared to one in 1,000 individuals in the non-Asian U.S. population. Approximately 40 percent of chronic HBV cases are among Asian Americans, although they comprise only 4 percent of the U.S. population. As a result of chronic HBV infection, Asian Americans are 2.7 times more likely to develop liver cancer than Caucasians and 2.4 times more likely to die from the malignancy.

While there is no cure for chronic hepatitis B, there are tools available to diagnose, prevent and treat the condition. As in Ma's case, a simple blood test can determine infection and for those not infected, there is a vaccine to inoculate against the virus. Those already infected can utilize several treatments to reduce their virus level and slow the progression of liver damage. Ma gave up alcohol to help preserve her liver, started a program of annual sonograms to monitor the disease, and received a hepatitis A vaccine. She also became active in a movement to make Asian Americans, Pacific Islanders and all segments of the population more aware of the risks and importance of prevention or treatment of the chronic infection.

Chronic HBV is difficult to eradicate because it causes few symptoms before the patient reaches the end stages of liver disease or cancer. In fact, a recent study found that up to two-thirds of Asian Americans with chronic HBV were unaware of their infection. The hepatitis B virus is found in the blood and other bodily fluids, such as semen, vaginal secretions and saliva. It can be spread through sexual contact and in childbirth as well as through sharing personal items such as razors and toothbrushes. Another transmission

route is the use of contaminated needles in drug injections, body piercing or tattooing.

In 2006, Ma sponsored a California bill aimed at making Medi-Cal coverage available for HBV screens, tests, vaccinations and treatment. "Currently," Ma noted, "Medical only covers hep B treatment when symptoms appear, and that's too late, when a patient's only option might be a liver transplant."

Although budget constraints defeated AB 158, Ma continues to look for ways to make the Asian-American community more aware of the disease and to encourage her constituents to seek screening, vaccination and treatment. The San Francisco Hepatitis B Free campaign (http://sfhepbfree.org), also organized by Stanford's Asian Liver Center, makes all of those options available, even to those without insurance coverage—and those fearful that by getting tested they will lose the coverage they already have. Ma said that the San Francisco Hepatitis B Free campaign is fast becoming a replicable model for other cities.

A safe and effective vaccine has been available for more than 20 years, and more than 1 billion doses of the vaccine have been administered worldwide. In the United States, routine immunization of infants, screening of pregnant women and vaccination at the time of delivery (for newborns of HBV-infected women) have greatly reduced infection at birth over the past two decades.

Still, today an estimated 2 million people in the United States are living with chronic HBV and more than 45,000 new infections occurred nationwide in 2006. The CDC recommends that all people in high-risk groups be tested and, when appropriate, vaccinated.

Although there is currently no cure for hepatitis B, drugs can slow its progression. Antiviral medications directly inhibit the replication of the hepatitis B virus. These drugs can be used long term with the intent of lowering the viral loads to such low levels that no further liver damage is caused.

The biotechnology and pharmaceutical industries continue to seek better treatments as well as a cure for the disease. Gilead's first treatment for chronic HBV, Hepsera, is one of the most widely prescribed oral agents for the disease in the United States. However, in August 2008, the company announced that Viread, a once-daily oral compound originally developed and approved for treatment of HIV, had been proven more effective than Hespera in treating chronic hepatitis B infections and was approved by the FDA for that usage.

Other California companies seeking to deliver better diagnostics, therapies and cures for the disease include Roche Molecular Diagnostics, which received FDA clearance in September 2008 to market the first test measuring hepatitis B viral DNA in blood samples with its Cobas TaqMan HBV test. Gen-Probe markets and continues to improve hepatitis B and C screening products to ensure the safety of the blood supply.

Ma reflects, "Asian society is very private about personal matters and, especially, what they see as health defects. Often, people don't want to know bad news, because they will have to deal with it. They have a fear of doctors, of insurance companies, and of how they'll be able to cope with a disease." She added, "I know a lot of people want me to stop talking about this, but if I can help save people's lives, I must do it."

Special Section: Diagnostics
Personalized Medicine Evolving in California

Richard Jove, Ph.D., is a pioneer in identifying STAT proteins as new molecular targets for cancer therapy. He joined City of Hope in August 2005 and was named director of Beckman Research Institute in January 2008. In addition, he is deputy director of the Comprehensive Cancer Center, co-leader of the Developmental Cancer Therapeutics Program and a professor in the COH Division of Molecular Medicine. Prior to joining COH, Jove served as director of the Molecular Oncology Program and associate director of basic research at the H. Lee Moffitt Cancer Center & Research Institute in Florida. Earlier in his career, he was a tenured faculty member at the University of Michigan Medical School in Ann Arbor, where he also served as director of molecular oncology. Jove, who has published more than 150 original research articles in peer-reviewed journals, has received numerous honors during his career, including the Damon Runyon-Walter Winchell Cancer Fund Postdoctoral Fellowship at Rockefeller University, the American Cancer Society Junior Faculty Research Award at the University of Michigan, and the Morsani Endowed Chair in Molecular Oncology at Moffitt Cancer Center. He earned his doctorate in molecular biology from Columbia University and received postdoctoral training in cancer research at Rockefeller University.

Personalized medicine is the concept that information contained in a patient's genotype or gene expression profile could help physicians prescribe the therapies most likely to help the patient and avoid those with little or detrimental effect. In clinical care, that means a doctor could use the personalized genetic information to determine the stage of disease, select among medications and other therapies, tailor dosages to best match the patient's needs, or initiate preventive measures to lessen the downstream damage of the disease or its treatment.

When the Human Genome Project completed mapping the human genome in 2003, investors and the general public expected that personalized medicine would manifest instantaneously. That has not been the case, although 10 targeted drugs have been approved since 2005,[1] and early and clinical stage drug development projects are gaining momentum in research labs across the country.

In a 2005 report, *Personalized Medicine: The Emerging Pharmacogenomics Revolution*, PwC interviews with thought leaders from across the drug development and healthcare provider spectrum yielded a number of predictions about the entry of personalized medicine into mainstream healthcare. The approach would be used first in oncology, where patients and their physicians are most motivated to try experimental drugs; where the disease is complex and highly variable from patient-to-patient; where researchers are most receptive to innovative and breakthrough technologies; and where funding for trials, studies and other research is most available.

Moreover, PwC noted that pharmacogenomics would dramatically change both medical research and clinical treatments. Using the human genome, drug developers would be better able to identify the genes and proteins that play critical roles in disease and design drugs specifically to inhibit or up-regulate those as needed. Companies would invent better diagnostics for more precise identification of the patient's condition and for use in preclinical and clinical testing. Statisticians would be better able to design clinical trials to demonstrate efficacy and to pinpoint the sub-populations most likely to benefit from the investigational new drug—and speed the path to market at the same time. And pharmacogenomics would enable earlier detection and possible prevention of disease.

The PwC predictions, which focused on a five-to-10-year timeframe, are coming to pass. Look no further than City of Hope (COH), the National Cancer Institute-designated Comprehensive Cancer Center in Duarte, Calif. "Personalized medicine is the future of cancer therapy," said Richard Jove, Ph.D., director of the Beckman Reserach Institute and deputy director of the Comprehensive Cancer Center at COH. "When you combine molecular biomarkers with targeted therapies, you get improved outcomes. You see both better clinical efficacy with the prescribed therapy and lower toxicities."

Jove explained that the term personalized medicine covers many different approaches to drug development and that the use of biomarkers multiplies the opportunities that researchers and innovators have in their quest to better treat and, indeed, cure cancer. For instance, the biomarkers themselves can be genes, which are essentially the blueprints for individuals' bodies. They can be embedded in

the mRNA, or the body's instruction manual for cell and tissue production. Or they can be found among the proteins that are the building blocks of the body. Cutting edge technologies are available and in use for screening and profiling these biological molecules.

Personalized medicine also promises to target different classes of therapeutics, including small molecules, antibodies, gene therapies and cell therapies. Of these, Jove said the small molecules remain the most widely pursued today. They can by derived from natural products, "as are about 75 percent of all cancer drugs currently," he said, or can be purely synthetic with no natural counterparts.

With Genentech's targeted cancer drugs, trastuzumab (Herceptin) for breast cancer and imatrib mesylate (Gleevec) for chronic myeloid leukemia and gastrointestinal stromal tumors, as an example the respective biomarker genes are the therapeutic targets. That is, the drugs alter the specific gene's or protein's activity in the body, which can diminish tumors and prolong life.

"The biomarker for Gleevec has been around for decades, and recognized as playing a causative role," Jove said. "But until Gleevec was approved, there was nothing oncologists or patients could do with that information."

In another targeted cancer drug, ImClone's cetuximab (Erbitux), the biomarker is the presence of the wild-type K-ras gene, which can predict positive response to chemotherapy-plus-cetuximab in two-thirds of colorectal cancer patients. Despite the strong correlation with the gene, Jove said, Erbitux acts on a different target: it is a recombinant monoclonal antibody to the epidermal growth factor receptor.

Using the tools and technologies of genomic research, drug developers can better identify and validate molecular targets. They also are better equipped to identify lead compounds, optimize their lead candidate, and inform their preclinical development activities and ultimately clinical trials.

In many ways, Jove said, personalized medicine is making drug development more complicated. Yet it is also further coalescing the parties that drive science while furthering the scientific knowledge base. "Traditionally," he said, "academia provided the basic research that would spark an idea for a new drug or therapy. That idea would be licensed to a drug development company for preclinical development and, perhaps, would come back to academia for clinical testing." In the new order, COH and other academic and independent research centers are also involved in target validation and the other research-intensive steps in drug development. Jove said that the working partnership for personalized medicine combines the expertise, funding and resources of government, industry and academia.

While Jove said this strengthened three-way partnership has the potential of driving faster, more efficient and safer drug development, some challenges to personalized medicine remain—all of them centered on funding. First, he said that NIH funding for research grants is "severely constrained." With the growing competition for fewer funds, "many promising grants that could have a major impact on cancer are not funded," he said.

Investigational new drugs that reach clinical trials are often stymied by insurers' reluctance to cover experimental drug therapies. "The high costs of clinical trials to academic medical centers is not widely appreciated," said Jove. Although the drug developer often covers some costs of the new drug and the clinical research staff, they may balk at covering standard-of-care costs if the patient also

is taking an experimental drug. Thus, many costs not covered by insurance companies or drug companies are borne by the medical center conducting the clinical trial.

Further, because personalized medicine automatically narrows the potential patient population, drug and diagnostics developers may not be able to recoup their development costs, much less generate the level of profit necessary to build value for shareholders and fund future R&D pursuits.

Jove works everyday against the challenges that cancer poses for researchers, clinicians, patients and caregivers. He says that finding better ways to diagnose and treat the disease is critical to all of those parties. It is also growing in importance to California: the state ranks number one in the nation for annual new cancer cases with nearly 157,000 projected in 2008. Among these new cases, breast, prostate and lung cancer are the most prevalent. The state also is at the top in the nation for oncology deaths per year.[2]

"In light of the costs in human life and suffering, the challenges of personalized medicine are offset by the potential benefits it offers cancer patients in terms of more effective and less toxic treatments," Jove said.

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1. Roan, Shari, "For cancer patients, personalized treatment offers a new range of options—and hope." *Los Angeles Times*. Oct. 20, 2008.
2. American Cancer Society, *Cancer Facts & Figures 2008*. Atlanta: American Cancer Society: 2008.

Mari Baker
President and CEO
Navigenics

Putting the "Personal" in Personalized Medicine

Navigenics is a Redwood Shores, Calif.-based genetic screening company. It runs a scan of each customer's genome, carried out by a government certified laboratory, that captures data on 1.8 million genetic risk markers. Navigenics compares individual results to reputable scientific and medical research before providing customers with personalized genetic risk estimates for specific, common health conditions and traits. The results are delivered via a secure online report that summarizes predispositions for a wide variety of cancers, cardiovascular conditions, gastrointestinal diseases, ophthalmic ailments, and more.

The predisposition data are supported by information and genetic counseling that customers can access 24-hours per day. Drawing on a wealth of genomic research that links genes to disease, Navigenics enables individuals to make lifestyle and environment decisions to prevent the onset of certain disorders.

The company's genetic counselors, medical advisors and health writers also provide tips on symptoms to watch for and the tests one might ask for in his or her annual physical to detect and diagnose rare diseases early in their development.

The program, called Navigenics Health Compass, includes ongoing, secure, personalized updates for an entire year. The customer's profile is updated as new information is discovered about genetic markers, certain conditions, and changing wellness strategies and therapies.

Larry L. Wood, MBA

PROFILE

Larry L. Wood is corporate vice president of transcatheter valve replacement at Edwards Lifesciences in Irvine, Calif. He earned his bachelor's degree in business from the University of Phoenix and his MBA from Pepperdine University. He completed his formal education through the company's continuing education program and augmented his training by holding progressively more responsible positions throughout the corporation. Wood joined Edwards in 1985.

As Corporate Vice President of Transcatheter Valve Replacement at Edwards Lifesciences, Larry L. Wood is responsible for every aspect of the company's new transcatheter heart valve replacement program. He oversees research and development staffs in Irvine, Calif. and in Israel, as well as the clinical testing, regulatory affairs, marketing and training activities around the innovative technology.

"Transcatheter valve replacement is one of the most exciting developments in cardiac therapy," Wood said. He explained that the technology, currently in clinical trials, is designed to enable doctors to compress a replacement heart valve around a balloon, which can be delivered via catheter. The catheter is threaded through a patient's leg artery into the diseased valve, and the balloon is inflated, implanting the new replacement valve. "This means that valve replacement would no longer require open-heart surgery," he said. "It would make valve replacements feasible for high-risk patients with co-morbidities that might preclude more invasive surgery." He said the transcatheter valve replacement recipient would be expected to spend a few days in the hospital before returning home—without requiring the assisted care or long recovery times associated with major surgery.

Wood joined American Hospital Supply Corporation, a predecessor to Edwards, straight out of high school. At the time, the company was focused on *in vitro* diagnostics, and Wood assembled blood chemical analyzers. Baxter purchased American Hospital Supply in 1986 and spun out Edwards Lifesciences 14 years later. Wood has progressed through the organization's various functions and earned his degrees with the company's assistance. "Most people go to college to get a job," he said. By securing the work first, however, he was able to apply his night schooling directly to his day job.

His career path has been unconventional, too, in that he has held positions in manufacturing, regulatory affairs and clinical marketing. "It's been a great education to have worked in these different groups and to understand the viewpoints and motivations of each," he said. Regulatory affairs, for instance, must be conservative and carefully manage risk, whereas the marketing team is focused on presenting the product's benefits. "We work in multidisciplinary teams, and understanding those natural tensions [between departments' functions] means we can work together to develop and deliver the best possible products for patients."

Cardiovascular product development is not just Wood's job; he says it's his passion. "Here you see so directly how your work applies to real patients," he said, "and that's a remarkable thing. Some of our patients are children with congenital heart defects. There isn't anything more rewarding than to be able to give someone their son's or daughter's health back."

He enthusiastically recommends the biomedical industry to anyone who is passionate about helping patients. "There will always be unmet patient needs," he said, "especially in cardiovascular medicine, given our aging population…I feel very blessed and very fortunate in that I get to do work that motivates and excites me every day."

Special Section: Diagnostics
Pinpointing Minute Differences

Daniel O'Day
President and CEO
Roche Molecular Diagnostics

Henry L. Nordhoff
Chairman and CEO
Gen-Probe Incorporated

Personalized medicine, or using one's individual genetic information to help guide diagnosis and therapy, is a promising yet complicated business. The complexity starts with diagnostics, a field producing amazing insights along with challenging puzzles.

Diagnostics Overview

Diagnostic technologies are tools that help physicians diagnose and better characterize their patients' condition. These include *in vitro* diagnostics (IVDs)—literally "in glass," as on a slide or in a test tube. These tests are conducted in a controlled environment outside a living organism. Among the older and most familiar are pregnancy tests, cholesterol screenings, blood tests and more. IVDs are commonly used to protect the blood supply, monitor levels of administered drugs and provide information to help healthcare professionals diagnose and treat disease. These tests can be run in hospital and other pathology labs, in doctors' offices and, increasingly, by patients themselves.

Molecular diagnostics, tests to identify a disease or predisposition for disease by analyzing DNA or RNA of an organism, are enabling research breakthroughs in labs around the world. In recent years, the diagnostics industry has developed highly sophisticated and innovative molecular diagnostics using technologies such as PCR (polymerase chain reaction) to identify the presence of viruses such as hepatitis and HIV, mass spectrometry and microarrays, which can screen thousands of markers in a patient's DNA. The technologies also are making the full spectrum of healthcare options—from predisposition screening to disease and therapy monitoring—increasingly available to physicians and their patients. Continuous advances in the diagnostics field are reducing the costs and time required to analyze an individual's complete genome, for instance, making more ambitious research projects possible. Genomics promises to make drug development faster and safer by enabling researchers to precisely identify the groups of patients who will respond to a new medicine.

As with any disruptive technology, however, not all components of the diagnostics sector are moving at the same speed. Scientists and researchers continue to expand the uses and capabilities of novel technologies. Entrepreneurs are commercializing diagnostic kits and services at a rapid pace. Consumers are beginning to request more extensive and precise tests to gauge their personal risk factors. But the healthcare system is still in the early stages of determining how to regulate diagnostic technologies and pay for their applications.

Regulatory Questions

Regulators are working to understand and keep pace with diagnostics. One challenge they face is that the sector has developed two separate regulatory pathways: diagnostics to be used in research and controlled laboratory settings are regulated by the Clinical Laboratory Improvement Amendments (CLIA), managed by the Centers for Medicare and Medicaid

Services (CMS). Congress passed amendments in 1988 to establish quality standards for all laboratory testing.

In contrast, all commercially marketed tests for clinical use are regulated by the FDA. The agency's rigorous standards require that the developer demonstrate that the tests are reliable, accurate and clinically relevant. Technology has advanced so quickly, however, that the criteria underlying FDA regulations are becoming outdated. For instance, early diagnostics looked for one marker within a patient's sample—e.g., whether or not strep throat was present. New molecular diagnostics, such as Luminex's Prodesse Proflu-1, may simultaneously measure multiple markers. The Prodesse Proflu-1 is a respiratory virus panel that measures for nine different cold and flu strains. FDA regulations are not so clear for proving the safety, efficacy and reliability of such complex tools.

Conflicts in the dual regulatory system occur when a test approved for research lab use finds its way into clinician or patient hands. In spring 2008, two such tests for an ovarian cancer biomarker were launched without FDA approval. The FDA pulled the tests off the market, yet the concerns these events raised remain. The most important concern is consumer safety.

Pressure is building for the FDA to begin the necessary planning to establish one set of standards that will better govern the diagnostics sector. The agency's mission is more than protecting public safety, it also includes improving public health. In order for new treatments and technologies to be developed and delivered to patients, industry regulations must be carefully crafted so that they protect innovation.

Reimbursement Issues

The breakthrough diagnostic discoveries and capabilities have come with a price. The industry argues that a test should be valued based on what it is able to save the payer, the patient and the physician in other costs. The financial and human costs of subjecting patients to ineffective treatments are enormous. For example, if a molecular diagnostic demonstrates that a cancer patient will not benefit from chemotherapy, a payer could save tens of thousands of dollars in chemotherapy, facility and follow-up care costs.[1]

Roche, Massachusetts General Hospital and St. Michael's Hospital in Toronto, Canada, ran studies that demonstrated the cost savings diagnostics could deliver. The researchers looked at the cost-effectiveness of using Roche's proBNP test, a simple blood test, on patients presenting in the emergency room with shortness of breath. This symptom can indicate heart failure, asthma, or the flu—conditions with entirely different prognoses and immediate treatment requirements. Roche's test helps physicians determine which patients must be hospitalized and which should go home to rest and drink plenty of fluids. The study with Massachusetts General included 599 patients and demonstrated that use of the proBNP resulted in better patient care, shortened hospital stays and total cost savings of $474 per patient. The St. Michael's study, conducted in seven hospitals, showed that using the test shortened the emergency

Timothy Wollaeger
Managing Director
Sanderling Ventures

Chris Neary
Vice President of Corporate Strategic Planning
Beckman Coulter

room visit by an average of 42 minutes. The test also reduced the number of patients hospitalized within 60 days from 51 to 33.

The debate about whether diagnostics should be priced on the value they deliver, the recovery of their development costs, or the sum of their materials and assembly is just beginning.

Theranostics Complexities

Theranostics is the fusion of drug therapy and diagnostics to optimize efficacy and safety—and to streamline, in theory, the product development process. Combining a drug with a diagnostic process or test is also known as companion diagnostics, integrated medicine, pharmacodiagnostics and Dx/Rx partnering. Whatever the label, such combination therapies represent the ideal goal of medicine: to tailor treatment to an individual patient's disorder.

Ideals are challenging to attain. Theranostics presents a "chicken-and-egg" conundrum. A diagnostic innovator does not want to develop a test for which no treatment is available. And a drug developer may not be able to demonstrate its investigational new drug's efficacy without a test to select the subgroup of patients most likely to benefit. Meanwhile, development timelines for the two products are markedly different—roughly 10 to 15 years for a new pharmaceutical and three or four years for a diagnostic. If a drug company proceeds through clinical trials with a CLIA-approved test, it faces delays in product launch while the FDA-sanctioned test is developed as well as questions about the validity of the test results given the different test. Neither party wants to take on the development costs of the diagnostic before the drug shows promise, and neither wants its product exclusively locked in with the other. In theranostics, the drug company and diagnostic provider face intense pricing

Figure 18: Rx/Dx Commercialization and Value

Source: Patrick F. Terry, Technic Solutions, LLC

negotiations with one another long before they have to sell their combination product to insurers.

Even as diagnostic companies are trying to untangle the many threads of this knot, they are contributing to personalized medicine using several different strategies.

Put the Chicken and Egg in the Same Nest

Daniel O'Day, president and chief executive officer of Roche Molecular Diagnostics in Pleasanton, Calif., does not worry about the tension between diagnostic and therapeutic innovation.

"Roche is one of the few global companies that has gathered pharma and diagnostics under one umbrella," he said. "It gives us a lot of synergies." He said his staff of about 1,200 people worldwide works on countless projects with their pharmaceutical colleagues in developing diagnostics to improve treatment outcome and quality of care, drive R&D, deliver clinically differentiated and efficacious medications, advance companion diagnostic programs and discover biomarkers for new development programs. Although the bulk of Roche Diagnostics' work is in partnership with Roche Pharma, O'Day said that his company also collaborates on diagnostics with other developers.

Among the innovations Roche Diagnostics has launched has been an HIV viral load test, which monitors viral levels or disease progression and therapy effectiveness, O'Day said. "By establishing a baseline level of infection, and monitoring viral load, the physician can better assess the individual's response to therapy." The company also offers viral load screening tests for hepatitis C and hepatitis B viruses. Some hepatitis C patients may have a shorter, more customized treatment duration with Pegasys/Copegasys by monitoring those patients who have low virus levels before starting treatment, and who show a rapid virological response by clearing the virus from the blood within the first four weeks of treatment.

The AmpliChip CYP450 Test is a Roche Diagnostics' microarray that monitors how patients metabolize drugs, a key to individualizing treatment among patients taking the same medication. Already launched in Europe and coming soon to the United States is a human papillomavirus (HPV) diagnostic test for women to detect 13 types of HPV, which can lead to cervical cancer. "This test is an improvement over Pap smears," O'Day said, "which are often less sensitive and do not distinguish genotypes."

Enlarge the Playing Field

Genomic Health, Inc., a diagnostics company in Redwood City, Calif. conducts sophisticated genomic research to develop clinically validated molecular diagnostics. The company's first testing device, Oncotype DX Breast Cancer Assay, was first clinically validated for women with stage I or II, node-negative, estrogen receptor-positive disease. The assay helps physicians predict which patients will best respond to tamoxifen, a widely used chemotherapy treatment.

In early 2008, Genomic Health broadened the assay's use to quantify the likelihood of

breast cancer recurrence based on the expression of 21 genes in the tumor. The test also predicts benefit from chemotherapy for an individual patient. Clinical studies of Oncotype DX in other populations are currently underway, and Genomic Health's research team is developing other oncogenomic tests to enhance patient selection for a series of treatments in cancer. The company believes such services would provide clinically validated, actionable information to improve the quality of treatment decisions for cancer patients.

Be Invaluable to Those Driving Better, More Cost-Effective Healthcare

Beckman Coulter, Inc., based in Fullerton, Calif., is a pioneer in the field of biomedical testing instrument systems, tests and supplies that simplify and automate laboratory processes. Of the top 50 world-changing inventions identified by the Chemical Heritage Foundation, 18 were developed by Beckman and one by Coulter–the firms merged in 1997.

"For the past 15 years, our goal has been to simplify, automate and innovate our customers' facilities," said Chris Neary, vice president of corporate strategic planning for Beckman Coulter. "Those customers include hospitals, core labs and research facilities, and our success has come from thoroughly understanding our customers' needs." Beckman Coulter supports these customer groups with clinical chemistry systems, blood cell analysis systems, immunochemistry systems, centrifuges, rapid test kits, and reagents.

Beckman Coulter manufactures more than 1,200 tests that provide essential information to physicians and patients. Neary pointed out that, "Diagnostic tests improve patient health, and they can save healthcare dollars," because with early detection and more appropriate treatment come better medical and economic outcomes. "Although diagnostics comprise only a small portion of total hospital spending—less than 5 percent—they influence up to 60 percent to 70 percent of healthcare decision-making," he added.

Yet Neary said that molecular diagnostics are only now beginning to become standard equipment in hospital labs. Beckman Coulter is developing a molecular diagnostic instrument targeted to the routine hospital lab and the specific requirements of that environment.

But the future is wide open. "In the next decade," he predicted, "we will each have our full genome recorded on a chip that we can carry around that our physicians will use to diagnose and treat us." He said that personalized medicine could make individuals more knowledgeable and proactive about their own healthcare. "We will also see the expansion of home-based testing and monitoring in our homes."

Do What You Do Best While Positioning for the Future

San Diego-based Gen-Probe Incorporated is a molecular diagnostics company that develops, manufactures and markets nucleic acid tests (NATs) that provide fast, accurate, cost-effective results based on the human genome. The company is perhaps best known for its ability to detect the unique genetic sequences of microorganisms that can infect donated blood. For example, Gen-Probe's tests for HIV-1 and

the hepatitis C virus have helped reduce the risk of contracting these dangerous diseases from a blood transfusion to approximately one in 2 million. The company's tests are also used to detect hepatitis B and the West Nile virus.

Gen-Probe's product portfolio applies the company's patented technologies toward detecting infectious microorganisms, including those causing sexually transmitted diseases such as chlamydia and gonorrhea; tuberculosis; strep throat; pneumonia; and fungal infections.

Hank Nordhoff, chairman and chief executive officer of Gen-Probe, firmly believes that the future of diagnostics is aligned with personalized medicine. "Diagnostic tests are an essential part of the healthcare process and provide critical information to physicians and patients. Diagnostics can help assess a patient's risk for disease, assist in the diagnosis of diseases, and help physicians determine what therapies or treatments are appropriate for a given patient."

Gen-Probe hopes to help make theranostics a mutually beneficial pursuit for pharmaceutical and diagnostics companies. In the meantime, the company is developing NATs to detect prostate cancer, HPV, and other diseases. Gen-Probe also is working with General Electric and Millipore to develop NATs that detect microorganisms that commonly contaminate industrial processes.

Convince Others through Your Success

Timothy Wollaeger, managing director of Sanderling Ventures, was the chief financial officer for Hybritech, San Diego's first biomedical company. Hybritech's diagnostic kits for allergies, pregnancy, anemia and prostate cancer set the bar for the industry. Wollaeger also helped found Biosite in 1998. The company developed several products for rapid and accurate diagnosis of critical conditions including drugs of abuse, congestive heart failure and heart attack.

"We started Biosite with $600,000 and sold it for $1.07 billion" to Inverness Medical Innovations, Inc. in 2007, he said. "Diagnostics is perceived as less lucrative [among life sciences companies], although Gen-Probe's and Biosite's market caps should change that perception."

Wollaeger is bullish on the future of the diagnostics sector. "Any time you offer a product or service that improves outcomes while lowering costs, you should find a market. If your product improves healthcare in a society with an aging population, you will succeed."

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1. Johns Hopkins health alert, "The High Cost of Chemotherapy—Survival comes dear for cancer patients who need some new anticancer drugs," advises that the most expensive chemotherapy cocktail could run from $20,000–$30,000 for the chemotherapy drugs alone. Accessed at: http://www.johnshopkinshealthalerts.com/alerts/prescription_drugs/JohnsHopkinsPrescriptionsDrugsHealthAlert_1053-1.html

Biomedical Manufacturing

When it comes to biomedical research and development, California offers some of the most sought after addresses in the world. Proximity to universities, investors, peers, infrastructure and professional support services make the Golden State's biomedical clusters the most productive centers for medical innovation. The climate, quality of life, culture, outdoor adventures and educational and career opportunities promise that California will continue to draw and retain some of the brightest and most ambitious minds in science, engineering, information technology, healthcare and investing.

Yet innovation and invention are only part of the biomedical value chain. If there is a weak link in California's dominance of the biomedical industry, it is manufacturing. Ten or 20 years ago, when California's emerging biotechnology and medical device companies began developing their manufacturing processes, they expected that their plants would be close by—at least close enough to be "in and out in a day." As communications technology has evolved, and costs have risen, companies are less concerned that all their operations be within a couple hours' drive of one another.

Add to that the assertive efforts by other states and countries to attract manufacturing facilities, and the responsibility California public companies have to shareholders to consider lower-cost options. Current financial strain will make manufacturing cost considerations all the more critical. In light of the state's unprecedented budget deficits, California legislators and policymakers will have a more difficult time than ever in keeping the state's manufacturing plants and jobs here at home.

According to the most recent PwC-CHI California Biomedical Industry Survey, the majority of respondents had expanded (40 percent) or held steady (53 percent) their manufacturing operations within the state in 2008. Only 7 percent had reduced their operations here. The survey, completed just as the financial crisis was unfolding, found that 41 percent of the respondents expect to expand manufacturing in the state in the next two years with 49 percent holding steady. Another 11 percent expect to reduce their California manufacturing activities in the coming two years.

Figure 19: CHI-PwC Survey: Has your manufacturing activity within California expanded, held steady or been reduced in the past year?

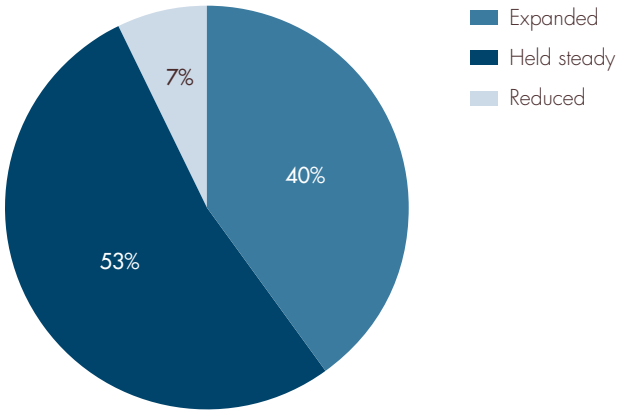
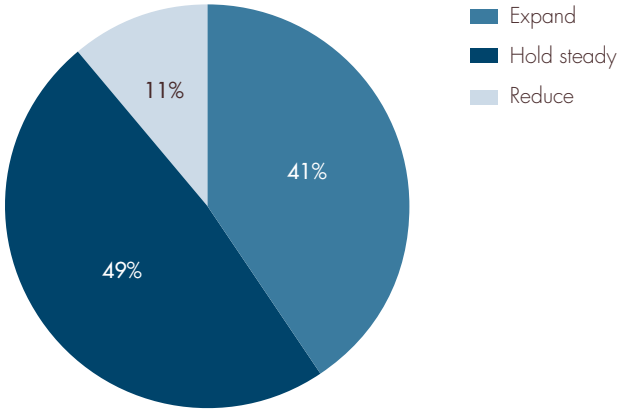
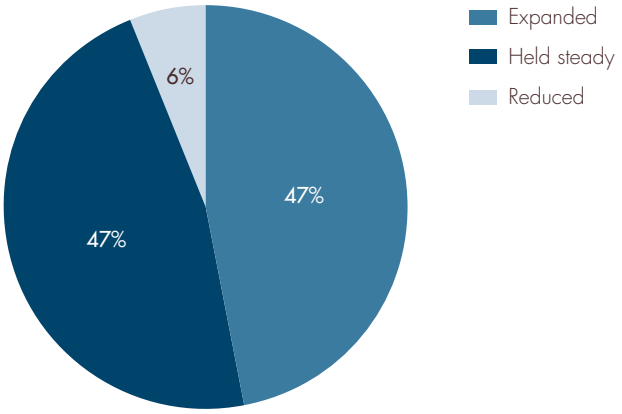


Figure 20: CHI-PwC Survey: In the next two years, do you expect your manufacturing activity within California to expand, hold steady or be reduced?



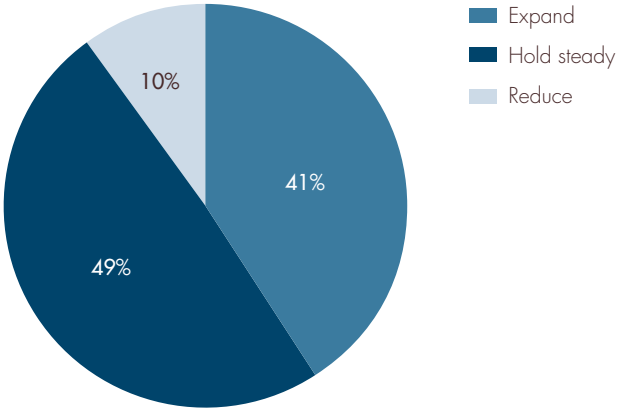
"Manufacturing activities" includes a number of metrics. When asked about manufacturing headcount, 47 percent of respondents said they had increased payroll in the past year and 47 percent said their rolls had remained steady. Six percent had reduced their manufacturing staff.

Figure 21: CHI-PwC Survey: Has your manufacturing headcount within California expanded, held steady or reduced in the past year?



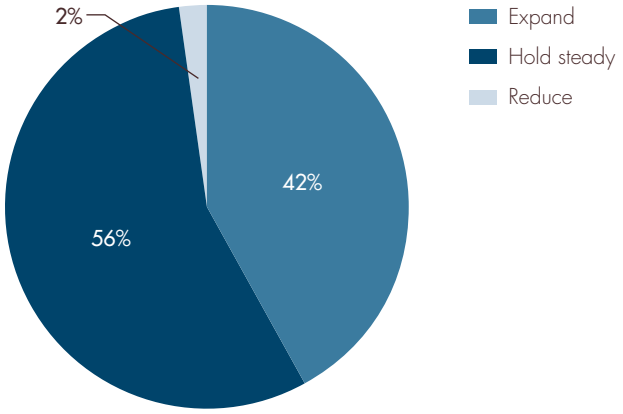
The outlook for the coming two years was less robust, with 41 percent expecting to add more manufacturing personnel and 49 percent anticipating no change. Of the respondents, 10 percent indicated they expected they would employ fewer manufacturing staff in California in the next two years.

Figure 22: CHI-PwC Survey: In the next two years, do you expect your manufacturing headcount within California to expand, hold steady or reduce?



Forty-two percent of the respondents do expect to expand their manufacturing activities beyond California's borders, however, and 56 percent will hold steady their out-of-state manufacturing activities. In contrast to in-state reductions, only 2 percent of the respondents expect to decrease their out-of-state manufacturing operations within the next two years.

Figure 23: CHI-PwC Survey: In the next two years, do you expect your manufacturing activity outside of California to expand, hold steady or reduce?



Among destinations mentioned by those who had or were planning to expand outside the state were regions (Europe, Southeast Asia, and New England); countries (India, China, Ireland, Japan, Mexico and Singapore, among others) and U.S. states (Florida, Massachusetts, Maryland, New York and Wisconsin). Without question, all of these competing locales have created alluring packages of economic incentives, lower costs, lower taxes and less restrictive regulations to tempt biomedical companies to manufacture, package and distribute products from their zip or mail codes.

The question of moving or staying requires a complex evaluation of interrelated advantages and challenges, costs and benefits. The factors are financial, political and strategic and may, in the end, not depend on any action or inaction by the state of California. In fact, companies themselves have created reasons to stay—many have worked closely with California's schools and colleges to tailor workforce training programs that address their particular needs. They have invested millions in their California manufacturing facilities. And they have established roots and expectations in their particular communities and with their California employees, all of which makes shuttering a facility here more difficult.

Still, preserving manufacturing operations—and the tax revenues, educational assistance, quality of life and infrastructure advantages they bring—in California is in the state's best interest. Successful biomedical companies provide the high-wage jobs and related state and local tax revenues that represent the best hope for economic growth in California.

Biomedical Manufacturing: Harvesting the Fruits of Our Labors

No place measures up to California as the address of choice for biomedical research and development. Make that addresses, given the San Francisco, Orange County and San Diego life sciences hubs. The state offers innovators, researchers, engineers, scientists and entrepreneurs the advantages of like-minded professionals, ready capital and world-class research institutions.

Yet once those innovators have negotiated the long path from concept to product, their expansion plans frequently take them to other states or countries to build their manufacturing and distribution centers.

"We're a California company," said Andrea Jackson, director of state affairs at Genentech. In March 2006, Genentech announced that it would site its new fill-and-finish facility in Hillsboro, Ore. The $350 million facility, to be fully operational in 2010, is expected to employ approximately 200 to 250 employees when it is licensed and operational in 2010. Genentech later decided to build a distribution center there as well.

Genentech's decision to expand out of state echoed numerous others before it. In 2005, Amylin announced that it would build its manufacturing plant for its type 2 diabetes treatment, Byetta (exenatide), in West Chester Township, Ohio. In May 2007, the company revealed plans for a $400 million-expansion there that would add an additional 500 jobs. According to Ohio's governor's office, those jobs average $50,000 per year. Further, they were not affected by Amylin's recent restructuring and layoffs in its San Diego R&D facilities and company headquarters.

Even companies that initially built manufacturing facilities in the Golden State have been changing their minds. In August 2008, Affymetrix released news of its plans to shutter its West Sacramento and South San Francisco plants and move operations to Singapore. The company said that the actions affect 100 jobs, though some of the employees would be offered other positions in the company. Affymetrix maintains manufacturing facilities in Santa Clara, Calif. and Cleveland, as well.

Also in August 2008 came news that Abbott Laboratories planned to eliminate 1,000 jobs in closing its South Pasadena facility. The company expected to realize annual savings of $150 million by transferring its operations to two Irish factories. According to the company's statement, the plant made liquid reagents for diagnostic tests for cancer, heart disease, diabetes and drugs of abuse. The unit had produced tests responsible for 12.2 percent of the company's 2007 sales.

Genentech's Jackson said that the decision to expand into Oregon hinged on California's corporate income tax structure. She said that California calculates corporate taxes based in part on the employees and facilities operating within the state. "If you add property and employees in California," she said, "your corporate taxes go up. If you add them somewhere else, your taxes here decrease." The company cited Oregon's single-sales factor apportionment tax policy as being particularly attractive.

Genentech does maintain a manufacturing plant in Vacaville, as do Johnson & Johnson

and Novartis. Vacaville's economic development manager, Michael Palombo, would like to attract more life sciences manufacturing to his city.

"Life sciences companies are in a growth industry," he said. "They build high-value properties, which improve our tax base. They need skilled employees." He said the companies have drawn skilled workers to Vacaville and established training programs for people already living in the area. "It's also a plus that they produce important products in clean plants. We feel good about having that here."

Palombo says Vacaville is not alone in seeking biomedical manufacturing, however. "We have been on the shortlist with Singapore," he said. "We're competing with countries. We're competing with states. We believe we offer companies a great deal in terms of location, labor force and incentives…But Vacaville can't compete with Texas or Iowa, much less China."

He said that California does offer workforce training assistance—up to $1,600 per employee—for new manufacturing operations. "The state is supportive of research but does not seem to have the same 'let's-get-it-done' attitude for manufacturing."

Palombo is not alone in that assessment. The Development Counsellors International (DCI), a public relations consulting firm that works with governments to attract new businesses, has found in three consecutive industry studies that California is not business friendly.[1] In 2002, 2005 and 2008, the state was cited as the least favorable in which to do business, with 72 percent of respondents feeling that way in 2008. And California ranked worst among all types of respondents in the survey: large company executives, midsize company executives and location advisors.

According to the report, "California was cited for having 'too much regulation and an anti-business climate' by 58 percent of respondents, while 37 percent mention 'high costs' and 28 percent said 'taxes.'"

Interestingly, two factors that place high on the list of desirable attributes for California's R&D operations—quality of life and proximity to funding sources—figured lowest among the DCI survey respondents. They instead weighed the labor force (a measure that included availability, quality and cost), overall operating costs and, in a near tie, efficient transportation systems or business-friendly government.

Jackson notes that the jobs that manufacturing brings could fill a particular niche in California. "Biomanufacturing creates hundreds of jobs for people with community college degrees or high school diplomas," she said. "There are currently a number of California companies on the cusp of introducing their first products. They can let their manufacturing go elsewhere." She added, "They can site their manufacturing jobs in other states."

California and the biomedical clusters have looked to entrepreneurs, engineers and researchers to drive business growth in their geographic regions. The approach has generated high-level, high paying jobs for thousands of professionals with advanced degrees. It also has resulted in support services that employ an additional three to five people for every biomedical employee.[2] And the innovation centers do perpetuate California's reputation as the home of new ideas.

Still, Palombo would like to see California retain the manufacturing and long-term operations that the successful startups will require. "A biopharmaceutical manufacturing plant is much better than research in terms of tax returns," he said. "One percent of a research facility valuated at $30 million is peanuts compared to 1 percent of a $1.2 billion assessed fill-and-finish plant." Manufacturing plants frequently upgrade their equipment, triggering new appraisals each time.

On behalf of the California communities pursuing biomedical manufacturing, Palombo said, "I don't necessarily expect the state to provide huge incentives to retain or recruit manufacturing. I just want it to stop with the disincentives."

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2. DeVol R, Wong P, Ki J, Bedroussian A, and Koepp R. America's Biotech and Life Sciences Clusters: San Diego's Position and Economic Contributions. Milken Institute. June 2004. Accessed at: http://www.milkeninstitute.org/pdf/biotech_clusters.pdf

Special Section: Orange County, The Med-tech Cluster

Orange County Highlights

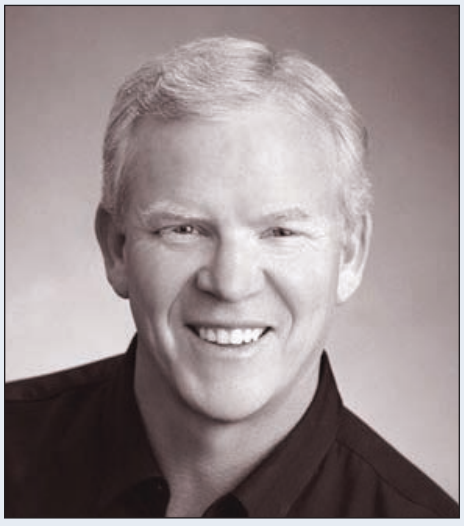
Total estimated employment: 29,000

Total estimated wages and salaries paid: $2.2 billion

Average wage: Nearly $76,800

Percentage of total California biomedical workforce: 11%

Statewide ranking: Third



William "Bill" J. Link, Ph.D.
Co-founder and Managing Director
Versant Ventures

Orange County: the evolution of a biomedical cluster.

The high-profile clusters of the San Francisco Bay Area, San Diego, Cambridge, Mass. and Research Triangle Park, N.C., share certain characteristics. All are home to world-class universities and research centers. All have developed technology transfer policies that allow breakthrough discoveries in basic science to be licensed for commercial development. And each has well-established companies that exemplify commercial success and provide a pool of managerial talent.

These clusters have blossomed because the key players are connected by common goals. Each has created an environment that supports startup companies with venture capital and networks of supplier and professional services.

Clustering in Orange County

"To use a metaphor, the Bay Area garden is flourishing," said Charles Baecker, director of The Don Beall Center for Innovation and Entrepreneurship at UCI's Paul Merage School of Business. "Orange County's garden, like our terrain, is more sparse, more a chaparral. We are a microclimate that is perfect for nascent startups in biomedical and IT discoveries."

Current Landscape

All told, the biomedical industry employed more than 29,000 people in Orange County in 2007. They earned annual wages of $2.2 billion at a weighted average of $76,800 for the year. Orange County employees make up nearly 11 percent of the total California biomedical workforce. The county ranks third statewide, behind the Bay Area and Los Angeles County.

Orange County is home to the University of California, Irvine, long recognized for its math, science and engineering programs. Its Paul Merage School of Business is quickly becoming a leading institution in the country, and work is underway to establish a world-class school of law.

The area's leading homegrown biomedical employers include Allergan, Edwards Lifesciences, Beckman Coulter, and Advanced Medical Optics, among others. Through acquisitions, global corporations such as Bausch & Lomb have established a presence in the county. And an estimated 300 small medical device companies (<15 employees) operate from San Clemente to Fullerton.

Among biomedical venture capitalists, Versant Ventures and its managing director, William "Bill" J. Link, Ph.D., operate from Newport Beach. Link is credited with helping to finance 20 biomedical companies, half of them in Orange County. Other investors across the state are well aware of the med-tech community here, too. Guy Nohra, co-founder and managing director of Alta Partners in San Francisco, said he covers about 30 companies in the corridor between Irvine and northern San Diego.

The relationships among business, academia and capital in Orange County have been and remain positive. "We all have a common quest of improving human health and life," said Michael V. Drake, M.D., chancellor of UCI. "The university is an excellent engine for innovation. To help people, those ideas have to be turned into products that are practical and can be delivered to patient populations." He said that the many collaborative efforts among the university and business community in Orange County have added to UCI's facilities and programs. By working with local

businesses, UCI has afforded its students relevant, real-world educational experiences.

"UCI really understands the meaning of partnership and of reaching out and engaging community leaders," said Michael A. Mussallem, chairman and chief executive officer of Edwards Lifesciences. "Edwards and UCI have had strong relationships in many areas like biomedical engineering, industry connections, student internships and graduate employment opportunities. As the university continues to grow and mature in areas of science, business and law, we anticipate many more opportunities for a global business like ours to benefit from."

Of his company's support of UCI, David E.I. Pyott, chairman and chief executive officer of Allergan, said, "We look at it from a holistic perspective: How do you create a strong infrastructure around you?" Since moving to Orange County in 1971, Allergan has seen and helped a "very strong industrial, research and educational community grow up around us," Pyott said.

Poised to Flourish

National Technical Laboratories, the original predecessor to Beckman Coulter, set up shop in Fullerton in Orange County in 1935. Allergan moved to Irvine from Los Angeles in 1971. Both companies have been generous and instrumental in supporting new departments and facilities at UCI. Even given those entities' decades of success here, many of the biomedical opinion leaders point to recent developments as harbingers of the OC medical technology cluster reaching critical mass.

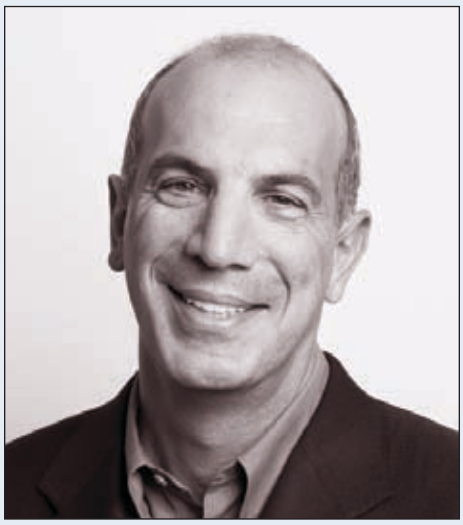
OCTANe is the leading innovation organization in Orange County with a mission to create, grow, support, staff and fund innovative biomedical and technology companies in Orange County and Southern California. So far, OCTANe has helped 23 companies raise more than $70 million in capital. The group's key initiatives include LaunchPad, which provide business and technical support, contacts, and access to capital for entrepreneurs and start-ups. OCTANe's program series draws close to 5,000 people each year, with the signature Medical Device Forum attracting more than 700 people from 350 companies worldwide. The OCTANe TalentEngine connects talented people with high-quality R&D jobs in OC through a robust portal with job opportunities, resumes, and private networking introductions. And finally, OCTANe kick-started the Okapi Fund, which closed in June 2006 with $30 million of private money to invest in local seed and early-stage companies.

Other developments also hint that Orange County's med-tech cluster will reach a new milestone in the near future. As described in the ophthalmology product development section of this report, Allergan and AMO also have been instrumental in planning and initiating fundraising for the $50 million Gavin S. Herbert Eye Institute, an ophthalmology training, research and clinical care facility to be named for Allergan's founder and former chairman. Organizers are raising money for the new institute, the bulk of which will come from private funds, and hope to break ground for the facility within two years.

The financial crisis of fall 2008 has lengthened the timelines but not diminished the aspirations of Orange County's business and educational leaders. David Schetter from UC Irvine's Office of Technology Alliances summed it up by saying, "The environment has made capital more difficult to acquire, but for good technologies with strong market potential, there seems to be enough money in the area to move forward, particularly when we do not need initially large sums of money." He added, "We are seeing, for example, investment groups that used to

Guy Nohra
Co-founder and Managing Director
Alta Partners

Michael V. Drake, M.D.
Chancellor
University of California, Irvine



Michael A. Mussallem
Chairman & CEO
Edwards Lifesciences

David E.I. Pyott
Chairman and CEO
Allergan

be in real estate syndicates, now looking into medical device company investments. There will probably be longer term effects as the financial environment continues to tighten. Overall, I would say that our plans have not changed and that good technology with high market potential will usually find the support it needs."

UCI's Baecker said, "I believe globalization hit OC manufacturing before other sectors of the national economy. We have been in a state of constant adjustment since the mid-1980s with many middleclass families starting a small service-based company to replace lost paychecks. As a consequence of 20 years of adjustment, we appear to be in a better relative position compared to other U.S. regions to weather the current economic storm."

Facing the Challenges

The financial crisis aside, Orange County does pose a few challenges for employers, educators and potential employees.

"The cost of living in Southern California is extremely high," said James V. "Jim" Mazzo, AMO's chairman and chief executive officer. "It reduces our ability to bring the best-qualified people in. We are competing against New York or New Jersey or the Midwest where salaries might or might not be lower but where housing will take a much lesser share of a paycheck."

Another challenge of a med-tech concentration is that the majority of the companies are quite small—15 or fewer employees—with personnel needs primarily in engineering and administration. The companies that do manufacture products employ 50 to 70 workers, according to Guy Nohra of Alta Partners. "When a company starts generating $40 to $50 million in product revenues," he said, "they often start looking to manufacture elsewhere." He said that Costa Rica, Puerto Rico and Ireland have been successful bidders on biomedical manufacturing jobs.

Further, Nohra said, the mark of success for a med-tech company is to sell its product line and/or technology platform to a larger player. If the acquirer is not also in Orange County, the jobs go away, at least until the entrepreneur launches a new company around the next idea. Cautioning legislators to beware of promoting policies with unintended consequences, Nohra said he knows of several med-tech inventors who took their proceeds to tax-friendlier Nevada to establish their next firms.

Carrying On

The beauty of being based in a biomedical cluster is that one is surrounded by people who understand one's ambitions and are willing to muster the resources to advance those dreams.

"Our headquarters are located in one of the largest medical device company clusters in the world," noted Mussallem, "which provides advantages when collaborating with local suppliers and partners, and by creating a larger pool of talent upon which we can draw."

"This is a wonderful place for what we do," said Drake. "We are working with energetic, creative people who are committed to making a difference. They are committed and passionate and appreciate the value of different points of view."

"The advantages of participating in Orange County's med-tech industry," said Link, "is that it is rich with entrepreneurs who've had a depth of experience. The county holds very strong academic institutions and affords good access to venture capital. The med-tech industry is stronger here than in any place in the world."

For these leaders, spring is coming to the chaparral.

Taiyin Yang, Ph.D.

PROFILE

Taiyin Yang, Ph.D., is senior vice president of pharmaceutical development and manufacturing at Gilead Sciences in Foster City. Yang earned her bachelor's degree in chemistry from National Taiwan University and her doctorate degree in organic chemistry from the University of Southern California. A member of the American Association of Pharmaceutical Scientists, the American Chemical Society and the Drug Information Association, she joined Gilead in 1993 from Syntex Corporation, where she was director of analytical chemistry.

Taiyin Yang, Ph.D., joined Gilead Sciences in 1993. At that time, Gilead was not the biggest or best-known company in the sector, but Yang focused on the potential. She knew and respected the senior management at Gilead, and appreciated their innovative approach to drug development. What's more, her new position had a broader scope of responsibility. "I saw it as an opportunity to make a difference at a company whose values very much mirrored mine. I saw the chance to help discover, develop and commercialize therapies for life-threatening conditions." Yang sites her experience as an example of the opportunities available in the constantly evolving biotech industry. "Learn, grow and you'll be rewarded with success of the company, then individually."

Yang expects that the life sciences job market will hold steady or grow in the coming years. She points to remaining unmet medical needs, an aging population, new discoveries in biology and technology, and continuing consolidation among biopharmaceutical companies as opportunities for talented scientists to find their niche.

At Gilead, Yang's chemists play a key role in project teams that take investigational new drugs from discovery to market launch. Her group manages the chemistry, manufacturing and control operations for the active pharmaceutical ingredients in Gilead's investigational and commercial products. They invent and develop the formulations for life-saving drugs, like Atripla, the first once-daily single tablet regimen for HIV-1 infection intended as a stand-alone therapy or in combination with other antiretrovirals.

By incorporating process development and formulation into the project team from the beginning, Gilead's approach creates process and cost efficiencies, and ensures that "our scientists are not just early discovery or mid- to late-stage development specialists," Yang said. "They are engaged through every phase of product development." She added that "The job is never the same. We never do drug development or chemistry the same way from one product to the other. We keep up with regulatory changes, changes in technologies and related scientific discoveries and use the latest developments to guide our work."

The one constant in Yang's and in Gilead's work is that "our true focus and passion is to deliver therapeutics to address unmet needs." In particular, Gilead's innovative combination therapies represent significant advancements in treatment–offering convenient once-daily dosing improved tolerability and fewer side effects for many people living with HIV. Yang said she is also proud of the company's mission of providing HIV therapeutics to "regions of the world that are resource-limited and where HIV/AIDS is prevalent." Gilead has developed a tiered pricing system for its HIV medicines, which offers no-profit prices—prices that reflect Gilead's cost of good and distribution costs—in more than 125 impoverished countries.

She said that Gilead's mission continually motivates her and is one reason that she fully recommends a career in the biomedical industry to young people. Her advice would be to appreciate that the work is complex and requires collaborations across many disciplines. "You need to develop a true level of expertise and in-depth knowledge in your area," she said, "and you have to be a resource to others." As for her own career, she says, "I wouldn't do anything differently, but I maybe would do more."

Academic Research

Basic research in university and independent academic research laboratories expands the foundation of scientific knowledge thereby serving as the launching pad for even more groundbreaking discoveries. Basic research sparks ideas for real world, real life therapies that can improve the health and lives of patients and their families.

Characterizing the replication mechanisms and lifecycles of viruses led to anti-infective medicines and vaccines, along with encouraging profound, yet simple, changes in human behavior to halt the spread of viral infections. Identifying ever-smaller subsets of cancer and their respective methods of thriving in the human body has spawned multiple arms of medical science aimed at addressing the disease. Describing and unraveling DNA's double-helix opened new pathways for genetic science, therapies and diagnostics.

Basic research is expensive, however, and commercial organizations, responsible for bringing new inventions to the marketplace, can seldom justify spending money on science that lacks a clear application. Thus basic discovery research is largely the province of universities. And for funding, research institutions look to government grants and charitable donations from foundations and individuals.

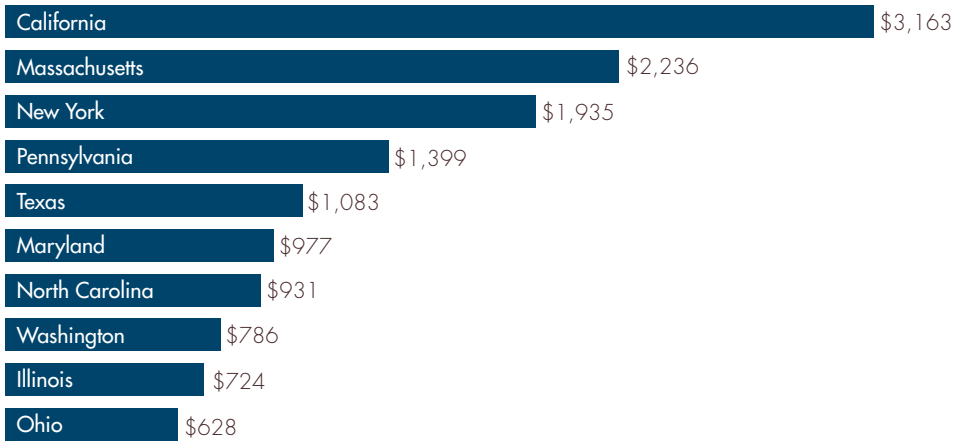
Grants from the National Institutes of Health

Since the 1950s, the NIH has been a major source of grant monies to universities and other researchers. The NIH encompasses 27 institutes and centers focused on the full breadth of health issues including oncology, cardiology, respiratory conditions, mental health, allergies, infectious diseases, aging and diabetes.

By enabling investigators within universities and independent labs to follow their passions in basic research, the NIH has transformed medicine. Its programs have made it possible for the United States' most gifted scientists and engineers to build careers in academia—and to guide the next generations in envisioning and finding their lifework in medical science as well.

The NIH was founded in 1946 and ever since, California's academic researchers have consistently been awarded more NIH funds than researchers in any other state. In 2007, California received 7,357 grants worth more than $3.16 billion. California collected approximately 41 percent more than the second largest grantee, Massachusetts. All 50 states receive some NIH funding, yet California collected 15 percent of total 2007 grants.

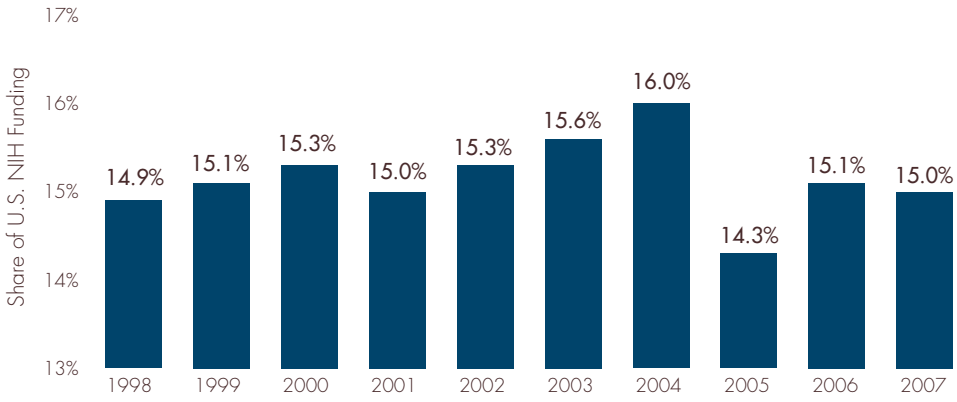
Figure 24: Top 10 NIH grant funding recipient states, fiscal year 2007



Source: National Institutes of Health, Office of Extramural Research

As shown in Figure 25, California's share of total U.S. NIH funding has remained fairly steady in the 15 percent range. The numbers from 2004 and 2005 are skewed by a $393.7 million Science Applications International Corporation (SAIC) grant that the research center received in 2004. The receipt bumped California's percentage of all NIH funding to 16 percent in that year. When SAIC transferred the grant to another facility out of state in 2005, California's share decreased to 14.3 percent.

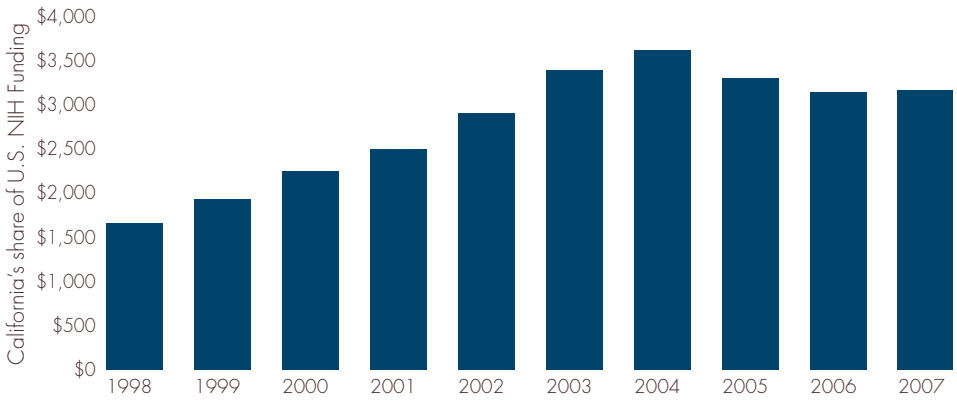
Figure 25: California's share of total U.S. NIH grant funding, fiscal years 1998 to 2007



Source: National Institutes of Health, Office of Extramural Research

Between 1998 and 2003, NIH funding to California more than doubled in nominal dollars (Figure 26), in line with national increases in NIH funding. Beginning in 2005, however, NIH funding to California decreased. When adjusted for inflation (in real terms), the 2007 funds fell back to 2003 levels.

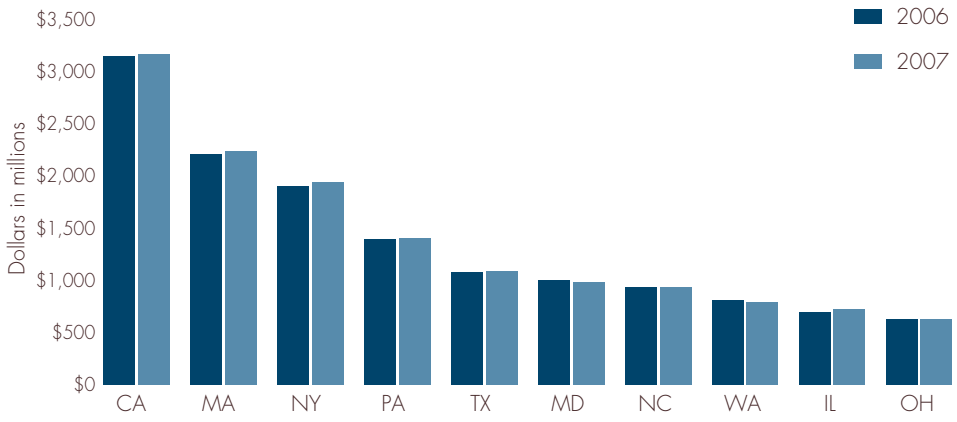
Figure 26: California's NIH funding, fiscal years 1998 to 2007 (millions of dollars)



Source: National Institutes of Health, Office of Extramural Research

All states consistently received less funding from 2005 to 2006. As shown in Figure 27, funding remained virtually flat for every state from 2006 to 2007.

Figure 27: Top 10 NIH grant funding recipient states, fiscal years 2006 and 2007 (millions of dollars)



Source: National Institutes of Health, Office of Extramural Research

Nearly 96 percent of the $3.16 billion that California researchers received in 2007 funded research projects. The remaining funds, or approximately $160 million, were divided among fellowships, training and construction grants (Figure 28).

Figure 28: Dollar amounts of California's NIH grants in 2007, by grant type

Grant Type	Dollar Amount (millions)	Grants Awarded
Total	**$3,163.3**	**7,357**
Research grants	$3,038.8	6,525
Training grants and fellowships	$117.8	805
Training grants	$96.6	301
Fellowships	$21.2	504
Construction grants	$1.3	2
Other awards	$5.4	22

Note: Numbers may not sum to total due to rounding.
Source: National Institutes of Health, Office of Extramural Research.

Training awards are designed to support the research training of scientists for careers in the biomedical and behavioral sciences fields. They also help professional schools establish, expand or improve their continuing professional education programs. The NIH-funded fellowships support individuals in their training goals. Training grants and fellowships are critical for supporting the excellence of biomedical institutions' educational programs and the caliber of their graduates. These grants, however, have decreased as a share of total NIH funding in recent years (Figure 29). Nationally, funding declined from 3.9 percent in fiscal year 1998 to 3.7 percent in fiscal year 2007, and from 4 percent in 1998 to 3.7 percent in 2007 for California.

Figure 29: NIH grants, total and training in fiscal years 1998 to 2007 (millions of dollars)

1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
United States									
Total grants									
$11,136	$12,804	$14,721	$16,701	$18,947	$21,669	$22,552	$23,117	$20,813	$21,067
Training grants and fellowships									
$430	$513	$546	$593	$657	$722	$749	$765	$758	$778
Training as a percent of U.S. total									
3.9%	4.0%	3.7%	3.6%	3.5%	3.3%	3.3%	3.3%	3.6%	3.7%
California									
Total grants									
$1,662	$1,933	$2,248	$2,497	$2,905	$3,386	$3,613	$3,301	$3,143	$3,163
Training grants and fellowships									
$67	$81	$83	$89	$97	$108	$114	$116	$111	$118
Training as a percent of California total									
4.0%	4.2%	3.7%	3.6%	3.3%	3.2%	3.2%	3.5%	3.5%	3.7%

Notes: Training awards are designed to support the research training of scientists for careers in the biomedical and behavioral sciences, as well as help professional schools to establish, expand, or improve programs of continuing professional education.

Fellowships are an NIH training program award where the NIH specifies the individual receiving the award.

Data are in nominal terms.

Source: National Institutes of Health, Office of Extramural Research.

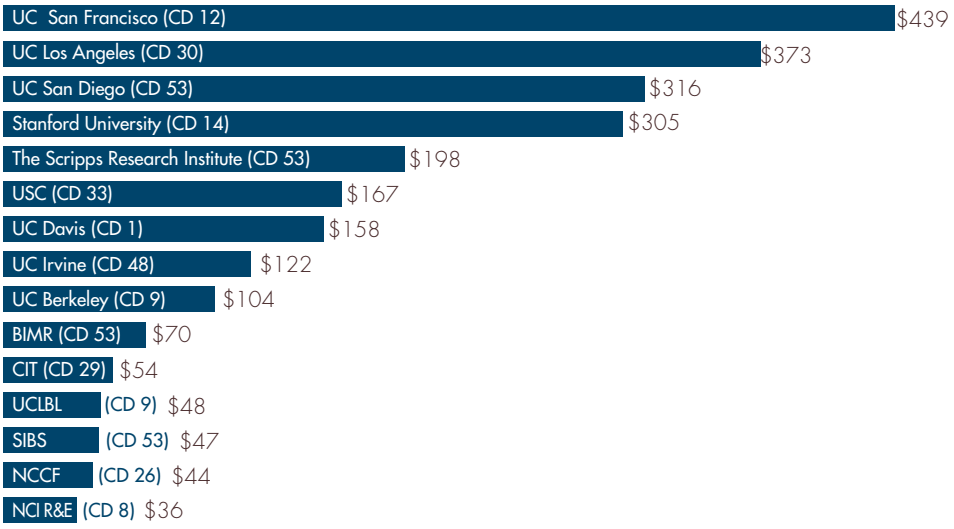
* Does not include research and development grants.

As shown in Figure 30, 10 of the top 15 recipient institutions in California in fiscal year 2007 were universities. Three of the top four were from the University of California system—UCSF, UCLA and UCSD. Stanford University rounded out that list. Of the independent research organizations, The Scripps Research Institute received the largest sum of NIH grants at $198 million. The Burnham Institute for Medical Research ($70 million), Salk Institute for Biological Studies ($47 million), National Childhood Cancer Foundation ($44 million), and Northern California Institute of Research and Education ($36 million) rank second through fifth, respectively, for independent research organizations.

California has 53 U.S. congressional districts. In fiscal year 2007, the 53rd District near San Diego received nearly 9 percent more NIH funding than any other district in the state with $734 million. The 53rd District is home to the Scripps, Burnham and Salk institutes as well as UCSD, San Diego State University, SAIC and others.

Following the 53rd District in total funding was the 12th District, which includes UCSF; the 30th District, home of UCLA and the

Figure 30: Fifteen largest NIH grantee institutions (with congressional district) in California in fiscal year 2007 (millions of dollars)



Source: National Institutes of Health, Office of Extramural Research

Cedars-Sinai Medical Center; the 14th District, which features Stanford University; and the 9th District, site of UC Berkeley.

Small Business Adminstration Programs

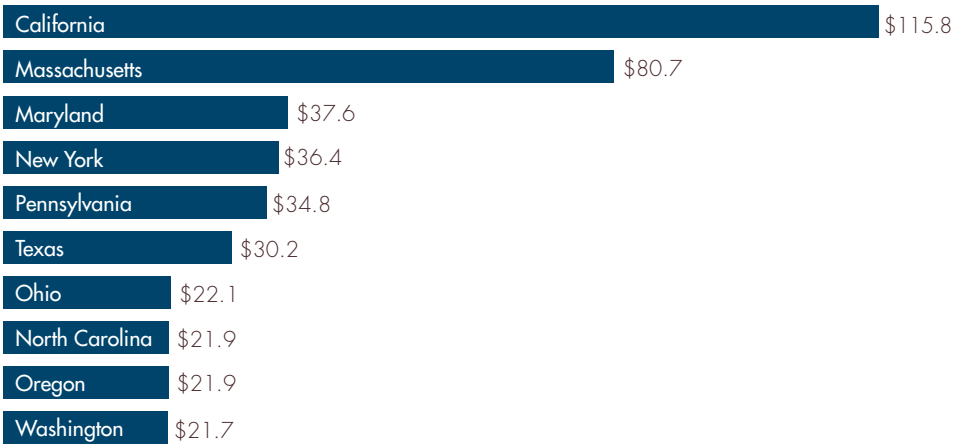
The NIH is not alone among government agencies supporting biomedical research and startups. The U.S. Small Business Administration's (SBA) Office of Technology uses two grant programs to increase the competitiveness of small, high-technology firms.

The first, the Small Business Innovation Research (SBIR) program, provides critical seed capital for biomedical entrepreneurs and often provides initial funding for start-up companies. Under the SBIR program, federal departments and agencies with annual extramural R&D budgets exceeding $100 million must reserve at least 2.5 percent of those budgets for awards to small U.S. high-tech firms.

Under the second program—Small Business Technology Transfer (STTR)—federal departments and agencies with annual extramural research budgets exceeding $1 billion must reserve 0.30 percent of such funds for awards to small U.S. high-tech firms. These awards are smaller than the SBIR grants and fund cooperative R&D projects involving small business and a nonprofit research institution.

Attracting NIH SBIR and STTR dollars can be critical for the development of new biomedical products, and California companies have been particularly successful in that regard. In 2007, the state received the largest number of NIH SBIR and STTR awards (amounting to 315) and the largest amount of total funding (nearly $115 million) in the United States. This number is a slight decrease from the previous year in which NIH SBIR and STTR awards totaled $118 million.

Figure 31: Top 10 recipients of NIH SBIR and STTR Funds in fiscal year 2007 (millions of dollars)



Source: National Institutes of Health, Office of Extramural Research

Technology Transfer Opportunities

The basic research discoveries made at California's and other U.S. universities and colleges via NIH grants often seed companies that can turn ideas into products that improve patients' lives. Through the federal Bayh-Dole legislation, federally funded institutions are able to transfer their technologies to commercial companies. In addition to serving as an added and much needed revenue generator for institutions, technology transfer has continued to feed innovation at the state's biotechnology, biopharmaceutical, medical device and diagnostics companies.

Among the companies responding to the CHI-PwC survey for this report:

- 27 percent credit a California academic or research institution for playing a central role in the creation or growth of the company
- 32 percent credit a non-California academic or research institution for playing a central role in the creation or growth of the company
- 30 percent have at least one patent license agreement with a California academic institution
- 44 percent have at least one patent license agreement with a non-California academic institution

Academic and commercial organizations frequently partner in another key way as well: through contract research. Such agreements can cover clinical and R&D research and are popular among the respondents to the CHI-PwC survey. In fact, of those participating:

- 54 percent had at least one clinical research or sponsored research agreement with a California academic research institution
- 58 percent had at least one clinical research or sponsored research agreement with a non-California academic research institution

Academic Research: University of California's School of Global Health

Haile T. Debas, M.D., is executive director, UCSF Global Health Sciences. The Maurice Galante Distinguished Professor of Surgery, Debas is also dean emeritus, school of medicine and vice chancellor emeritus, medical affairs, and chancellor emeritus. A native of Eritrea, he received his doctorate of medicine degree from McGill University and completed his surgical training at the University of British Columbia. Prior to becoming dean he served as chair of surgery at UCSF for six years. Under Debas' stewardship, the UCSF School of Medicine became a national model for medical education, an achievement for which he was recognized with the 2004 Abraham Flexner Award of the Association of American Medical Colleges. Debas also spearheaded the formation of several interdepartmental and interdisciplinary centers of excellence and was instrumental in developing UCSF's new campus at Mission Bay. He currently serves on the United Nations Commission on HIV/AIDS and Governance in Africa and on the Committee on Science, Engineering, and Public Policy of the National Academy of Sciences.

Some problems—world hunger, climate change and pandemics, to name a few—are so complex that solutions require a paradigm shift, a novel approach that sees the problem from a new angle of vision. A major effort to reconceptualize global health is under way in the in the University of California (UC) system.

One of the largest public research university in the world, UC is drawing upon its 10 campuses; great strengths and diversity in science and social science; five medical centers; schools of the health professions, engineering, business and law; and a statewide division of agriculture and natural resources to establish a system wide School of Global Health.

"Global health is not 'international health,'" explained Haile T. Debas, M.D., executive director of UCSF Global Health Sciences. "Global health issues are those that are as important in California as they are in other countries. Local health is affected when drug resistance develops anywhere in the world. Pandemics are a clear problem for Californians regardless of where the virus first mutates." Poverty, chronic diseases, aging, food and water security, disaster response and the effects of population movement on health are real issues in California and the U.S., as well as abroad.

"The underlying vision," Debas said, "is to extend our academic mission. Traditionally, we have been charged with education, research and dissemination of knowledge. The School of Global Health's added objectives will include instilling leadership skills and identifying projects that enable our students to take action and implement policy that make a real, beneficial and lasting impact on human health."

Academic activities will take place on several different campuses through Centers of Expertise (COE). Each of the five or six COEs will be developed around a theme related to a major global health challenge, such as poverty; migration and health; chronic diseases; food and water security; and disaster response. Campuses interested in becoming COEs are drafting proposals and will be selected on a competitive basis.

Each of the COEs will provide local administration; master's and doctorate programs related to their themes; interdisciplinary, problem-based research opportunities; and partner relationships with international, academic, industry and other non-governmental organizations. Students will be able to participate in interdisciplinary groups across the UC system.

Debas envisions a public-private partnership, noting that Gilead Sciences has underwritten several COE workshops. UC has received a $4 million, two-year grant from the Bill and Melinda Gates Foundation to plan the school.

Debas hopes to have approval for the School of Global Health from the UC Board of Regents in 2010—and to begin preparing students to start addressing global health issues, one problem and project at a time, shortly thereafter.

Tech Transfer: Bringing Innovations to Patients' Lives

Uday N. Kumar, M.D., a cardiologist and cardiac electrophysiologist, is the founder and chief medical officer of iRhythm Technologies, Inc. His venture-backed San Francisco medical device company develops devices and systems for cardiac rhythm monitoring. He is has also served as an adjunct clinical instructor of Cardiovascular Medicine at Stanford University, where he previously was a Biodesign Cardiovascular Innovation Fellow. Prior to Stanford, Kumar completed fellowships in cardiac electrophysiology and cardiology at the University of California, San Francisco (UCSF). He completed his training in internal medicine at Columbia-Presbyterian Hospital of Columbia University after earning his medical doctorate at Harvard Medical School and his bachelor's degree in biochemistry at Harvard College.

While still in medical school, Uday N. Kumar, M.D., began looking for ways to apply his passion for technology toward helping patients. He joined a group of friends, to help implement a way to use CAT scan and MRI imaging data with rapid prototyping techniques to make models for use in medical education and in planning surgical procedures. He took a year off between medical school and his residency to pursue the project and helped start Biomedical Modeling, Inc. The Boston-based company continues to make models to help surgeons visualize and master complex procedures.

Through that experience, Kumar started planning his life's work—work he knew would have to combine his love for cardiology with his passion to apply technology toward making a real and immediate difference in patients' lives. With its strength in med-tech, California provided the ideal place to accelerate his aspirations. He came to UCSF, and completed his fellowships in cardiology and cardiac electrophysiology, the branch of cardiology focused on arrhythmias, or abnormal heart rhythms.

With his medical training nearly complete, he applied for and was granted an Innovation Fellowship in Stanford's Biodesign Program. "The program is built on the premise that med-tech innovation can occur by following a rigorous process to understand unmet medical needs," Kumar said. "Innovation may be best enabled when bringing together viewpoints in a collaborative perspective." He explained that his team included three other members. One held a business degree, one had a doctorate in electrical engineering, and the third had earned a master's degree in mechanical engineering.

The team worked together for a year focusing on cardiac electrophysiology. They first made observations to discover hundreds of unmet needs in this space. They were aided by the fact that this was Kumar's specialty and an area of strength for the team's electrical engineer.

They next analyzed their findings to determine which needs they should prioritize. "As people age, arrhythmias increase in prevalence," Kumar said, "and with Baby Boomers aging, the burden of arrhythmias is only going to increase." However, despite this trend, he said that arrhythmias are still often poorly diagnosed. "People feel something funny. They might be dizzy or out of breath." He said the symptoms often do not send patients to a cardiologist, and they may even forget to mention the experience to their physicians. "Literally millions are not being diagnosed when they first complain about symptoms. Given that some can lead to worsening symptoms or even sudden death, ensuring that all arrhythmias are diagnosed is very important since the majority are treatable" he added.

The team then brainstormed approaches to addressing their opportunities and prototyped some aspects of a new concept for monitoring a person's heart rhythm. As part of learning

more about the field, the team members learned about protecting intellectual property, financing technology development and negotiating the regulatory pathway.

Kumar said that the Biodesign Program does not measure its success in the number of companies that are formed through it since the program's goal is to teach a process for understanding and solving problems. "But at the end of the fellowship, you do face a big decision: Do you feel strongly enough about this idea to take it forward?" He said his teammates pondered the idea and whether starting a business would fit into their lives and plans at the time.

The business degree holder took a position in sales at a large medical device company. The electrical engineer joined a mid-size startup company as a member of its R&D team. The mechanical engineer returned to school to complete a Ph.D. Though taking a risk, Kumar gave himself six to 12 months to determine whether he could take the rudimentary concept for the team's heart monitor and develop all the other elements needed so that it could be funded, built and commercialized.

Today, Kumar is chief medical officer of the company that grew out of his fellowship, iRhythm Technologies, Inc. in San Francisco. Founded in late 2006, iRhythm licensed the technology from Stanford and will pay milestones and royalty payments to the university and the other product inventors. The company is backed by venture capitalists, employs more than 25 people and has gained FDA approval on its first device. Kumar said they are now building a sales force to begin commercialization.

Kumar entered the Biodesign Program to learn to think "outside the box." He said, "The biggest thing I learned was to understand what I'm good at, what I don't know and what I want to spend time learning more about. I also learned about the importance of working with others with different backgrounds."

Today he spends most of his time at iRhythm and one day per week at Stanford, where he is helping to write a book about the Biodesign process. He also mentors and teaches in a collaborative program between Stanford's Biodesign Program and the Indian Institute of Technology and All India Institute of Medical Science. In that program, called Stanford-India Biodesign, fellows selected from India spend seven months at Stanford and five in India and work using the Biodesign process to understand and solve unmet medical needs specific to India. He also said that he would like to get back to seeing patients part-time. He said he misses interacting with patients, which he thinks is the best way to continue to understand unmet medical needs.

In other words, Kumar is not just thinking outside one carton. He's found a way to apply his training, skills and insights in all of his favorite boxes.

Academic Research: The PSM Program at California State University

Dr. Gail Naughton, dean of the College of Business Administration at San Diego State University, earned her doctorate in basic medical sciences, from St. Francis College, her Master of Science degree in histology from New York University Medical Center and an executive master's of business administration degree from the University of California, Los Angeles. Naughton sits on the scientific and industry advisory boards of leading universities and is on the boards of directors of the California Healthcare Institute, the San Diego World Trade Center and the San Diego State University Governance Institute. She serves on the boards of DermTech International, C.R. Bard Inc. and SYS Technologies Inc.

Employers in the biomedical sector face two significant challenges in building their workforce. The first is to spark an interest in science, mathematics and engineering in young people. The second is to make sure that prospective employees with mathematical and scientific backgrounds have the requisite business skills to succeed in industry, government or non-profit organizations.

Recognizing the importance of the latter challenge, the Alfred P. Sloan Foundation—a philanthropic institution based in New York City—launched its Professional Science Master's (PSM) initiative in 1997. The PSM is an innovative, new graduate degree designed to enable students to develop workplace skills highly valued by employers while pursuing advanced training in science or mathematics. PSM programs consist of two years of academic training in an emerging or interdisciplinary area, along with a professional component that typically covers topics such as communications, business fundamentals, project management and intellectual property. Instead of writing a thesis, PSM students complete an industrial internship.

Currently, 115 PSMs are offered through 60 U.S. colleges and universities. All of the offered PSM degrees have been developed in concert with industry and are designed to complement present and future professional career opportunities.

The California State University (CSU) system received its first Sloan Foundation PSM grant, for $891,000, in 2006 and a second for $474,000 in June 2008. Currently, CSU offers 14 PSM programs at 12 of its 23 campuses. Another 16 programs are in the planning stages, and CSU expects to train approximately 1,050 science and technology professionals in the next five years.

Of the current and planned programs, more than a dozen are focused on the life sciences, with specialties including biotechnology, agricultural biotechnology, biostatistics, bioinformatics, clinical project management, medical physics, computational science, environmental science, ecological economics, forensic science and genetic counseling. Other PSM degree programs prepare technical students for careers in the electronics and energy industries, and in government.

"CSU offers the largest and the strongest PSM program in the nation," said Gail Naughton, Ph.D., dean of the College of Business Administration at San Diego State University. "We are very conscientious about keeping our curriculum current. In the life sciences industry, that means keeping up with changes in FDA regulations, with trends in the marketplace, with advances in technology and with employer needs and expectations."

As a scientist-turned-businesswoman, Naughton said that she has a personal interest in seeing business-focused training succeed for math and science students. "When you train as a scientist, you are trained to work on your own—to pursue your own hypotheses and research. In industry, you have to participate on and contribute to a project team. It can be difficult adjusting to a team approach and learning to appreciate what others are bringing to the table." She said clearing that hurdle in the PSM program will put graduates one step ahead in the job market.

Programs aim to produce business-savvy workforce to boost U.S. competitiveness

San Diego State University is expanding its programs to train more people to enter science and technology professions—a need that industry leaders call urgent for keeping the U.S. economy competitive.

The biomedical industry "is an arena where every second counts," said Naughton. She noted that it currently takes an average of 15 years and more than $1 billion to advance a life science product from concept to customer. "A smarter workforce—one that is trained not just in science and math, but in critical business skills—can cut the time and expenses of bringing important new therapies to market. If you can commercialize your product sooner, you'll have that much more time in sales and product life."

Naughton believes that management and finance professionals cannot afford extra time to learn the life sciences business on the job. To help them get themselves up to speed while they are pursuing their higher education, San Diego State University and Kelley Executive Partners at Indiana University have developed the first ever MBA for Executives in Life Sciences (LSMBA) program.

The new program, which will enroll its first class in Fall 2009, offers a graduate degree online for the working biotech, medical device and pharmaceutical professional. The program is composed of 48 semester units of course work: 12 units of core business courses tailored to the life sciences industry; 15 units of managing innovation; 18 units of regulatory affairs courses; and three units of culminating experience. Designed to emphasize creativity, leadership and interpersonal skills, the LSMBA courses are structured sequentially so that faculty can build upon the concepts and skills presented in each preceding course. Teaching methodologies vary with subject matter and include classroom lectures, outside reading, case discussions, guest speakers and individual and small group projects. Many course assignments allow participants to apply the material directly to their professional experience.

The 20-month program begins and ends with two-week residencies in San Diego and also features a week-long residency in Indiana and a second, seven-day stay in Washington, D.C. In addition to interacting with one another, students will be matched to a mentor within the life sciences industry.

Naughton expects 35 to 40 students will join the inaugural class next summer. A pilot certificate program the schools ran enrolled 11 students from SDSU and 15 from Indiana University. "But given that the LSMBA is predominantly online, we will be able to serve life sciences professionals across the country," Naughton said.

Academic Research: SDSU's BioScience Center

San Diego State University's BioScience Center is a 35,000-square-foot research center that was conceived of by the faculty and constructed using private funding. The five-story structure opened in March 2006 with the first labs occupied that June. Still being built-out, the facility eventually will house 12 faculty members and a staff of 75 support personnel.

"Follow the science" is the mantra of researchers everywhere. For a group of biomedical investigators at San Diego State University, the motto led them to a new state-of-the-art research center. The SDSU BioScience Center (BSC) was built to address the microbial basis of cardiovascular disease.

Epidemiologic studies have shown a correlation between periodontal disease and atherosclerosis, or the build-up of plaque in arterial blood vessels. One line of ground-breaking research at the BSC seeks to quantify the cause-and-effect relationship between the two diseases. In fact, the investigators are conducting the first-ever study designed to show whether treating gum disease in young adults can postpone or even prevent the subsequent development of atherosclerosis.

The study is using a metagenomics approach to identify all bacteria and viruses that colonize the mouth, and bioinformatics analysis to determine whether specific organisms are associated with both atherosclerosis and periodontal disease. This comprehensive study will involve microbiology and cardiology investigators from SDSU and UCSD, dentists from USC and epidemiologists from the SDSU Graduate School of Public Health.

This study is expected to shed new light on an important aspect of health disparities, because the poor often have limited access to dental care. Neglected oral hygiene may increase the risk of heart disease, diabetes and complications of pregnancy, such as pre-term delivery, which are more prevalent among people with low incomes.

"A regular program of twice-yearly dental cleaning and regular tooth-brushing and flossing costs much less than a hospitalization for a myocardial infarction," said Roberta A. Gottlieb, M.D., director of the BSC and Frederick G. Henry Chair in the Life Sciences. "While drugs or diagnostic tests are often regarded as the tangible products of research, an equally valuable product is knowledge that leads to a beneficial change in public policy or human behavior. We expect that the findings from this study will point the way to a recommendation for routine preventive dental care in order to decrease the risk of developing atherosclerosis in later years."

Heart disease is one of the most pressing health issues affecting the industrialized world, yet the BSC is the first research center focused on the relationship between inflammation resulting from infection and cardiovascular disease.

In another study, the BSC will address the potential threat of Chagas Disease, a parasite endemic to Latin America that afflicts 20 million people. The risk of Chagas Disease, which leads to heart failure and intestinal complications, is on the rise in the United States because of increased immigration and global climate change that allows the insect vector to exist in more northern latitudes. "We also are concerned about the potential risk of acquiring Chagas Disease from ingesting imported fruits that may be contaminated with parasite-laden insects," Gottlieb said.

At present, only two drugs are available to combat the disease, and they have limited efficacy. No vaccine has been developed. Currently, SDSU is hosting a Fulbright Scholar from

Argentina, who will conduct research on the parasitic infection using a model system and reagents only available in the BSC. The BSC also is developing a screening test that can be used to ensure product safety.

In a third line of research, investigators are evaluating whether certain childhood viral infections might injure cardiac stem cells, which are required to help the heart grow and repair itself throughout life. If the stem cells are damaged, the heart has a limited ability to respond to stress such as hypertension or ischemia, resulting in a greater risk of heart failure. Investigators in the BSC have created the first animal model to test for this possibility and will be able to explore therapeutic solutions, possibly including vaccine development.

"Although acute bacterial infections are no longer the leading cause of death as they were 100 years ago," Gottlieb said, "they may contribute in subtle but substantial ways to heart disease—by triggering systemic inflammation or by compounding the damage mediated by genetics, lifestyle and the environment. We are just beginning to recognize the contribution to chronic disease by the complex microbial ecosystem that exists on us and within our bodies."

The BSC is approaching its mission by combining multidisciplinary basic science research, public health investigations and technology development. Gottlieb has brought together chemists, computational scientists, diverse biologists and epidemiologists to tackle these critical unmet needs.

"We will work closely with the biotechnology community in order to accelerate the transfer of knowledge from the laboratory to the commercial sector," Gottlieb said. "The greatest challenge we face is the funding gap between making the initial discovery and having a product ready to enter clinical trials. We will use the BioScience Center as a model system to explore innovative approaches to translational research as we move ahead with the mission to respond to the microbial causes of heart disease."

The BSC will be supported in this regard by SDSU's Technology Transfer Office, headed by Michael Rondelli. The Tech Transfer Office aggressively markets SDSU's intellectual property and continues to support the endeavor even after the licensing agreement is signed. "We will team up with experts in the biotech industry, including preclinical drug development, medicinal chemists and regulatory experts in order to shorten the time it takes to turn a discovery into a beneficial product," Rondelli said.

Academic Research: The Jackson Laboratory

Fueled by demand from California's early discovery research projects, The Jackson Laboratory plans to relocate its Sacramento facility (JAX—West) to new space in Sacramento in early 2009. At nearly three times the non-profit organization's current, 42,000-square-foot space, the new research center will enable JAX—West to grow its staff from 60 to nearly 200 within a year of the move. The staff includes a significant number of professionals with Ph.D., M.D. and D.V.M. degrees.

For nearly a decade, The Jackson Laboratory's JAX—West facility has supported the West Coast research community with novel mice that help scientists bridge the gap between discovery and clinical testing. The non-profit organization provides a local supply of mouse strains, mouse breeding and in vivo research services to support early discovery and pre-clinical research and development activities. JAX—West serves over 200 companies and academic institutions in California, alone.

To keep pace with the explosive growth in biomedical research—much of it fueled by California's stem cell research initiatives—The Jackson Laboratory is expanding. The new center will quadruple JAX—West's animal production capacity and offer more extensive breeding, in vivo, cancer and stem cell services, and greater customization of those services to meet specific research needs. Fully accredited, the expanded JAX In Vivo Services will support cancer research in addition to its current therapeutic focus areas. These include metabolic disease, such as diabetes; cardiovascular diseases; neurodegenerative disorders like Alzheimer's and ALS; and immune system disorders including diabetes, arthritis, inflammatory bowel disease and asthma.

The Jackson Laboratory is also launching stem cell research services using a unique mouse strain along with specialized services and training in stem cell implantation and model characterization. These new offerings align with and complement the direction in which the pharmaceutical and biotech community is headed.

"California leads the world in life sciences research and biomedical discovery," said Chuck Hewett, vice president and chief operating officer of The Jackson Laboratory. "Our mission to accelerate biomedical discovery by providing resources and services demands an expanded local presence in support of academic, biotechnology and pharmaceutical researchers." He added that the expanded JAX—West space, service offerings and professional staff demonstrate that "we are reaffirming our commitment to the California research community by investing in this new facility and the outstanding people who will raise our mice and provide quality research services."

Academic Research: California Entities in the NIH Roadmap Network

Soon after becoming the Director of the NIH, in May 2002, Elias A. Zerhouni, M.D. convened a series of meetings to chart a "roadmap" for medical research in the 21st century. His goal was to identify major opportunities and gaps in biomedical research that no single institute at NIH could tackle alone but that the agency as a whole could address to accelerate medical research. Developed with input from more than 300 nationally recognized leaders in academia, industry, government and the public, the NIH Roadmap includes initiatives to encourage new discovery pathways.

In September 2008, the NIH named nine centers selected for its new Molecular Libraries Probe Production Centers Network. These centers, located across the country, will use high-tech screening methods to identify small molecules that can be used as probes to investigate the diverse functions of cells. Small-molecule probes can be minutely targeted to interact with one site of a cell's chemical machinery, thus providing information on a specific step in a cascade of cell functions. In some cases, small molecules may have activity that gives them potential for eventual therapeutic as well as research use.

The network will use laboratory tests used to screen for specific types of probes to screen a library of more than 300,000 small molecules. These molecules are maintained in the program's Molecular Libraries Small Molecule Repository. All data generated by the screening will be available to public and private researchers through the new PubChem database. In other words, the consortium of national screening centers gives researchers in academic institutes, nonprofit organizations and small biotechnology companies access to ultra-high-throughput screening (HTS) capabilities. Until recently, HTS was primarily used by large pharmaceutical companies.

Three California organizations are playing prominent roles in the network, which will be funded at approximately $70 million annually over the four-year production phase.

The Scripps Research Institute (TSRI) in La Jolla is home of The Comprehensive Center for Chemical Probe Discovery and Optimization. Under the direction of Principal Investigator Hugh Rosen, the Scripps center will split its six-year, $80 million grant between its campuses in La Jolla and in Jupiter, Fla. The center will deploy its expertise in chemistry and biology, as well as its rapid-fire robotics testing system, to identify new targets in the body that play a key role in disease.

The Burnham Center for Chemical Genomics (BCCG), part of the Burnham Institute for Medical Research also in La Jolla, is the designated comprehensive center for chemical genomics. There, Principal Investigator John Reed , M.D., Ph.D., will work with researchers to either screen their HTS-ready assay against the full NIH Molecular Libraries Small Molecule Repository or to develop assays for targets that could lead to the development of novel, small-molecule probes. The BCCG provides scientific investigators with the tools to advance their projects through the complete chemical probe development process—from assay development to chemical synthesis of potent and selective probe compounds. BCCG also will use its six-year NIH grant—valued at $97.9 million—at its La Jolla campus and its new state-of-the-art ultra-HTS facility in Orlando, Fla.

Since 2004, the Molecular Libraries Small Molecule Repository has been housed at BioFocus DPI, a drug discovery research company in San Francisco. In September, the NIH extended its contract with BioFocus until December 2010 for an added contract value of $9 million. The facility acquires and stores compounds under the contract and distributes the compounds to the network's centers for high-throughput biological screening.

In addition to the grants supporting the research centers in the network, the NIH is funding individual investigators' basic research on new targets and probes that help scientists figure out what role the targets play in disease. The individual researchers will be assigned to the research center that has the expertise to best support their projects and will be allowed to collaborate with scientists at the research centers.

The California Institute for Regenerative Medicine Begins the Medical Revolution Promised Under Proposition 71

Alan Trounson, Ph.D., is president of the California Institute for Regenerative Medicine in San Francisco. Prior to joining CIRM in January 2008, Trounson was professor of stem cell sciences and director of the Monash Immunology and Stem Cell Laboratories at Monash University, where he retains the title of emeritus professor. He also founded the National Biotechnology Centre of Excellence—'Australian Stem Cell Centre.' A fellow of the Royal College of Obstetricians and Gynaecologists and an honorary fellow of the Australian and New Zealand College of Obstetricians and Gynaecologists, Trounson was awarded an honorary doctorate by the faculty of medicine at the University of Brussels. He has been a pioneer of human *in vitro* fertilisation (IVF) and associated reproductive technologies; the diagnosis of inherited genetic disease in pre-implantation embryos; the discovery and production of human embryonic stem cells and of their ability to be directed into neurones, prostate tissue and respiratory tissue.

Within two years of beginning operation, the California Institute for Regenerative Medicine (CIRM) funded scientists have produced more than 50 landmark publications in top biotechnology and science journals; and already one of CIRM's groups has moved into clinical trials. It is amazing that within such a brief time CIRM is meeting some of the long-term milestones set out in its 2006 Scientific Strategic Plan. CIRM's global leadership in stem cell science is now unquestioned and collaborative agreements to accelerate the science and leverage California funds have begun to coalesce. Victoria (Australia), Canada's Cancer Stem Cell Consortium, the Juvenile Diabetes Research Foundation and the Medical Research Council in the UK have signed agreements to collaborate in ways that will broaden and deepen the resources focused on discovery, translation and clinical application of pluripotent and progenitor stem cell technologies.

CIRM began operations on borrowed funding secured by California Governor Arnold Schwarzenegger and bond anticipation notes from donors who had supported Proposition 71. Robert Klein and his colleagues battled through more than two years of lawsuits trying to upend Proposition 71 and stall the fledgling CIRM agency. Remarkably, Klein succeeded in fending off these challenges and securing an agency not subject to political or ideological interference. At the beginning of 2007, CIRM began operating at full capacity with all the required advisory groups and its Board, the Independent Citizens Oversight Committee (ICOC), with 29 members drawn from patient advocacy, academic medical institutions, business and the general community. ICOC members are appointed by legislators and officers of the state. Founding President of CIRM, Zach Hall, Ph.D., and Interim President, Richard Murphy, Ph.D., established rigorous and robust operating procedures and a strong managerial structure for CIRM, which made Alan Trounson's introduction as CIRM President in January 2008 a relatively easy transition.

CIRM has provided 165 principal investigator scientists from all over California, with basic research grants to ensure the intellectual capital is focused on stem cell biology and biotechnology. Those investigator awards along with training and planning grants bring the total allocated to research programs within the major academic and medical research centers to more than $343 million. In addition, CIRM has awarded 12 new research institutes, centers and programs with capital to develop new buildings and shared laboratories. They will all be completed by 2010. The $271 million allocated by CIRM for these projects has been leveraged with more than $500 million raised through donations and institutional contributions. These facilities will result in California attracting a massive infusion of new researchers. These scientists are coming from other states and countries, and include people of

extraordinary accomplishment. Some of the world's best known stem cell scientists have even relocated part-time to join the energy that is being generated by such major new activity in the field. The ripple effects of new construction and scientific movement into California will have a major impact on boosting research institutions, biotechnology companies and the state's general economy. There is also a movement of major pharmaceutical companies with regenerative medicine interests into California. CIRM is looking to build partnerships among different institutional and commercial sectors to enable translation and clinical applications involving stem cell therapies.

By December 2008, CIRM expects six to eight biotechnology companies to be awarded research grants and believes this will help accelerate the further productivity of the California biotechnology industry. Policies relating to CIRM loans are almost completed and loans are expected to be available to the commercial sector by early 2009. At this time, the call for applications for "Disease Teams" will be released which is a major allocation of $120 to $200 million for six to 10 integrated teams who believe their research is so advanced that they can achieve an Investigational New Drug Application (IND) within four years. This is an ambitious program, but CIRM believes California can rise to the occasion and provide the agency with a range of potentially exciting proposals that have real clinical potential. It takes both basic research and applied R&D to bring innovative science to patients, and I would expect that most applications will include a commercial partner in the team.

"I recognize that there remain many potential obstacles in the long pipeline to the clinic," Trounson said. Not the least of which may include regulatory requirements, particularly for therapies that involve dosing patients with cells rather than drugs, the need to monitor patients for a long time and strategies for "tracking" the administered cells. CIRM is engaging immunologists to work on "tolerance" and immune suppression and expects to make this a major area of interest alongside stem cell biology. There are also fundamentals of financing necessary to address the large number of clinical trials expected. Investors may find it difficult to understand the business model that might be required for cures evolving from cell therapies. At the same time, small molecules that are identified by research in stem cell assays could be expected to pass through the normal biotechnology and pharmaceutical pipeline and California is very well placed to take advantage of this.

The time has come for the aspirations of Californians for a new medicine based on stem cell research to come into focus. CIRM is optimistic it will facilitate this next revolution in medicine. "We are well prepared for the task ahead," Trounson said.

Real Estate

Joel S. Marcus

Alexandria Real Estate Equities, Inc. develops and operates offices and laboratories, and owns approximately 160 properties housing biotechnology, pharmaceutical and medical device companies; research institutions; government agencies; and related service providers. The real estate investment trust (REIT) has an asset base of more than 13 million square feet that is concentrated in high-tech hotbed areas, including Mission Bay, South San Francisco, San Diego, Seattle, Research Triangle Park and Washington, D.C. Joel S. Marcus became the company's chief executive officer in March 1997 and has served as a director since the company's inception in 1994.

Expediting life science's natural clustering tendency, Alexandria Real Estate Equities, Inc. has specialized in developing all-encompassing research parks. The developer's strategy is to put university facilities and biotech companies, venture capitalists and device inventors within close proximity to one another—along with the employee base and public services all rely upon.

Since 2005, the Pasadena-based real estate investment trust has been committed to its flagship development—the Alexandria Center for Science and Technology at Mission Bay. The 303-acre plot was, until a decade ago, a landfill, Southern Pacific rail yard and warehouse district. When completed in 2011, the Bay Area development will include 13 laboratory and office facilities totaling approximately 2.7 million square feet.

The Alexandria Center is organized into four campuses around the University of California San Francisco (UCSF) hospital complex. Among marquee tenants is Pfizer, which in August selected the Alexandria property for its new Biotherapeutics and Bioinnovation Center (BBC). The BBC is a biotech-like unit Pfizer created with the staff from Rinat Neuroscience, which Pfizer acquired in 2006. Agreeing to a long-term lease of essentially all of the west campus, Pfizer is expected to move about 100 employees to the complex starting in early 2010.

Other notable tenants either housed or committed to moving into the development include Merck & Co., FibroGen Inc., biotech pioneer Bill Rutter's portfolio of companies, and the J. David Gladstone Institutes. Biotech venture capitalists have also signed on—Versant Ventures, Novo Ventures and Arch Venture Partners are leasing space on Owens Street.

"To succeed in life sciences," said Joel S. Marcus, Alexandria's CEO, "requires four strengths. You must have an accessible and supportive location. You must have a robust talent base. You need capital, whether that is provided by venture capitalists, NIH grants or pharmaceutical company partners. And you need world-class science." He said market forces do eventually bring all of those components together; but Alexandria's master-planned Mission Bay cluster is designing collaborative opportunities into the blueprints.

Building a research cluster from the ground up also enables the developer to incorporate cutting edge solutions to environmental and infrastructure use concerns as well. Marcus noted that the Mission Bay center is served by the Third Street Light Rail, the Caltrain

Station, Bay Area Rapid Transit (BART), multiple busses and large parking garages. Public transportation will be a viable option for the thousands of employees who will make their way to the Alexandria Center in coming years.

Marcus also is proud of the development's attention to the Leadership in Energy and Environmental Design (LEED) Green Building Rating System guidance. "We are working to meet all of the LEED standards in our structures and in sustainable operations. Ultimately our goal is zero-energy buildings. We aren't there yet, but the day is coming when our structures will not draw upon the power grid at all."

Acknowledging that companies are being very careful in the current financial environment, Marcus said, "Real estate is a lagging economic indicator, so we won't be able to fully quantify the trends until the end of next year. Once we get through this crisis, however, California will still be a great location for life sciences operations."

1500 Owens Street, Mission Bay

455 Mission Bay Blvd. South, Mission Bay

249 East Grand Avenue, South San Francisco

Real Estate: Genentech's South San Francisco Facility Runs Green

Genentech's South San Francisco Facility

Genentech has long been regarded as one of the more progressive companies in the biomedical industry. That reputation is furthered by the company's commitment to growing and operating in the most eco-friendly manner.

In 2007, Genentech's Corporate Engineering group developed a Sustainability Design Checklist based on The Leadership in Energy and Environmental Design (LEED) Green Building Rating System. The checklist is intended to guide the company in deploying new construction elements and daily operating practices that conserve energy, water and materials while also providing a reasonable return on investments.

The checklist is in full use in the company's South Campus development program. Genentech has identified a number of ways to build energy-efficiencies into the three new R&D buildings that form Phase II of the South Campus development. The new buildings will have variable primary flow chilled water systems to reduce power needed to drive pumps. Economizer fans will be installed to recirculate air and reduce cooling load in the summer and to use outside air to cool the buildings during the spring and winter. The buildings will also incorporate fan wall air handling systems, which eliminate the need for sound traps and are more efficient than traditional systems. The buildings will also use solar shading devices and white roofing materials as well as orienting buildings to minimize the impacts of midday summer sun to control solar gain.

Genentech insists upon high recycle-content building materials and integrates water-conserving systems throughout its campuses to help achieve its own 2010 corporate water use and greenhouse gas reduction goals.

Genentech's eco-friendly design philosophy extends beyond its building walls. The company has developed a comprehensive approach to design that relates site planning, building design and landscaping to the natural environment, respecting the integrity and biodiversity of natural systems throughout its campuses. By landscaping with native and drought-tolerant plants and controlling rainwater runoff, Genentech is helping to reduce its use of clean water for irrigation and to redirect rain water to irrigate its landscape and regenerate the local groundwater systems.

Because of prior use of the land by shipyards and paint and chemical manufacturers, a few of the properties required environmental remediation before they could be built upon. Genentech has worked to restore the natural flora and terrain as part of its construction program. The campus also includes part of the Bay Trail. The company is contributing to the trail as it grows, providing public access to the shoreline and amenities such as picnic tables and parking.

To help limit its impacts on the local community, Genentech strives to concentrate its growth on sites served by existing infrastructure. The company has been recognized, in fact, for the ways it has successfully encouraged employees to use alternative transportation. The company supports car pools, van pools and free commuter shuttle service from the South San Francisco BART and CalTrain, as well as various locations in San Francisco, and employees may also participate in the pre-tax commute program to purchase transit tickets. For added convenience, BART, Muni and CalTrain tickets are sold on campus.

Real Estate:
Arena Pharmaceuticals Builds "Green"

Arena Pharmaceuticals, a San Diego biopharmaceutical company, is completing its new Sorrento Valley building. The building's specifications exceed California's Title 24 energy efficiency standards by 30.9 percent as calculated by San Diego Gas & Electric (SDG&E). It is also expected to qualify for Leadership in Energy and Environmental Design (LEED) gold certification. LEED is a points-based system developed by the U.S. Green Building Council to standardize the "green" label. Buildings can be certified silver, gold or platinum based on points made from their energy efficiency.

Arena Pharmaceuticals' rooftop solar panels

Arena's eco-friendly, five-story building features a 1,207-panel solar system that covers the 45,000-square-foot roof. The system has the capacity to produce energy for the structure's interior lights as well as enough excess electricity to power 250 homes for SDG&E.

The building's roof is coated with 3.5 inch-thick white foam. The material insulates the building and sheds water even as it reflects solar rays, keeping the structure cooler than a traditional dark roof would. The company also made use of solar tubes to bring natural light into the inner office areas to further conserve energy.

Arena selected sound-proof windows to muffle jet plane noise from the nearby Marine Corps Air Station Miramar. The energy-efficient windows also block heat from coming in and prevent climate-controlled air from seeping out. The building's custom, state-of-the-art air conditioning unit further increases control over airflow within the building and Arena's ability to realize energy savings.

The cost of building green is estimated to be about 5 percent more than that of traditional construction. However the additional expense is offset, at least in part, by energy savings as well as incentive rebates. Arena expects to receive $91,000 from SDG&E and $461,000 from the California Energy Commission in incentive rebates for the green building design and the solar panel system. Also, energy-efficient enhancements should enhance the building's future resale value.

Construction of this building took 12 months, and Arena plans to build an additional four-story green building in the coming years.

Source: Johnson, Tony. "San Diego Bio-tech firm goes green." *The National Herald*. Sept. 9, 2008. Accessed at: http://www.thenuherald.com/home/index.cfm?event=displayArticlePrinterFriendly&uStory_id=753b2b23-e6d6-4cd0-8df3-60a3744cfa34

Conclusion

California's biomedical industry, as this report documents, has been both a powerful engine of economic growth and a rich source of innovative treatments for our worst diseases. Recent events have demonstrated, however, that no industry is immune to the financial contagion that has swept global markets into deep recession. If President Obama's stimulus recovery plan gains traction and succeeds in stabilizing the economy in 2009, there may be cause for optimism about 2010 and beyond. Yet even if a surge of government deficit spending turns things around, the biomedical industry is unlikely to go back to business as usual.

The industry's growth during the past quarter-century depended on ready access to capital, on government investment in basic research, and on the willingness of payers–mainly public and private insurers–to pay for leading-edge technologies. Most economists agree that two huge bubbles, the first in stocks, followed by one in housing, created an unsustainable credit environment in the U.S. and around the world. After the collapse, without access to credit, businesses and consumers have lost confidence and cut back spending. As a result of declining economic activity, California's annual budget deficit has soared past $40 billion. Meanwhile, the federal deficit may surpass a trillion dollars.

Government deficits will weigh heavily on research budgets and even more heavily on entitlement spending. In this climate, it is reasonable to argue that the president's economic recovery plan should include the NIH, which in the long term has fueled tremendous commercial investment in the life sciences. Because they are the basis of intellectual property and the source of our workforce, academic research and education must rank as the highest priority for state and federal government.

Government programs' coverage and reimbursement policies, beginning with Medicare and Medicaid, strongly influence the market for innovation. One potential consequence of today's historically unprecedented combination of deficits, bailouts and stimulus spending is an equally unprecedented federal effort to reorganize the American healthcare system. President Obama has committed his administration to covering the uninsured and reforming the health insurance market. No matter how this is achieved, it will entail drastic changes in the market for drugs, devices and diagnostics. The question for the biomedical industry is whether the future market will continue to offer sufficient returns to attract the next generation of risk capital.

The current drought in the capital markets makes this question all the more acute. Nervous institutional investors, searching for assets they regard as secure, have discounted high tech companies across the board. Biotech, device and diagnostics companies have not escaped the carnage. Even if the economy turns around in a year or so, where will the capacity for a surge in venture capital and startup funding come from?

While the answer to this question is far from clear, the biomedical industry's essential value, to human health and enterprise, is beyond doubt. Still, rebuilding the industry in the next stage of the U.S. economy is bound to be a drawn-out, difficult process, and one that demands a level of economic and political ingenuity commensurate with the scientific creativity that originally inspired us.

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Methodology

Survey

PricewaterhouseCoopers, with support from the California Healthcare Institute, administered a survey for the 2009 California Biomedical Report.

The survey was conducted in the fall of 2008 and targeted approximately 1,500 companies that conduct business in California in the areas of pharmaceuticals, biotechnology, medical devices, diagnostics or medical equipment.

PricewaterhouseCoopers provided a secure and confidential web-enabled questionnaire. Participants' data was captured by the web site and loaded into a database, which was then downloaded for formatting and analysis by PwC staff.

A total of 119 individuals from 107 companies participated in the survey.

Respondents by sector:

- Medical Devices: 23%
- Biotechnology: 25%
- Pharmaceuticals: 11%
- Diagnostics: 7%
- Laboratory Supplies or Services: 9%
- Bioinformatics/Information Technology: 1%
- Other (e.g., clinical research): 24%

Employment

Data

The data used to estimate employment in California's biomedical industry are made available by the California Employment Development Department (CA EDD), available at http://www.labormarketinfo.edd.ca.gov and the Bureau of Labor Statistics (BLS) Quarterly Census of Employment and Wages, available at http://www.bls.gov/cew/home.htm. These data are based on the Current Employment Statistics (CES) survey. The CES survey summarizes monthly employment, hours, and earnings data from a sample of California employers.

It does not include the self-employed, unpaid family workers, or private household employees. Jobs are counted regardless of full-time or part-time status. Individuals who hold more than one job may be counted more than once.

Employment data from company specific Securities and Exchange Commission (SEC) filings were also used to estimate employment in the biomedical industry, specifically for the medical device, instruments, and diagnostics sector.

Company filings with the SEC can be obtained from the EDGAR database available at http://www.sec.gov/edgar/searchedgar/webusers.htm.

The sectors of the biomedical industry that are used in this analysis are comprised of several

North American Industry Classification System (NAICS) codes which are assigned to sectors based off the description of the NAICS provided by the U.S. Census Bureau. Companies are assigned a single NAICS code by the Census Bureau, and therefore a company which manufactures both pharmaceuticals and medical devices would only be classified in one of these sectors depending on which is the primary production of the company.

Methodology

Wages were computed using the BLS data described above, available at http://www.bls.gov/cew/home.htm. The most recent year for which wage and employment data is available for the publication of this report is 2007.

Methodology

CA EDD employment data is broken down to the 6-digit NAICS code level. The relevant 6-digit NAICS code data are multiplied by the percent of the biomedical industry that is represented in the NAICS code, as derived by PwC from Census Bureau data. The methodology behind biomedical employment and wage tables in this year's report differs from previous years. In past years, PwC estimated narrow industry categories based on broader industry statistics which were available in the most recent year. This year, PwC was able to use more detailed, industry specific (6-digit NAICS code level) data. Although this makes this year's data not comparable to previous estimates, the new data is a more accurate portrayal of California's biomedical industry.

NIH Grants

Data

Data for this analysis comes from the National Institutes of Health Office of Extramural Research, available at http://grants.nih.gov/grants/oer.htm.

The data includes all awards to California from NIH, some of which do not necessarily fund basic biomedical research. For example, some grants were used for training programs and projects that are designed to support the research training of scientists for careers in the biomedical and behavioral sciences, as well as to help professional schools to establish, expand, or improve programs of continuing professional education. Other grants were used to fund health policy or behavioral science research. Despite these caveats, overall the NIH grant funding demonstrates the federal commitment to health science research in California.

Data comes in two forms:

1. State and Congressional District
   Source: http://report.nih.gov/award/trends/State_Congressional/StateOverview.cfm

2. NIH SBIR and STTR grants
   Source: http://grants.nih.gov/grants/Funding/award_data.htm

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The California Healthcare Institute

The California Healthcare Institute is a non-profit public policy research organization for California's biomedical R&D industry. CHI represents more than 250 leading medical device, biotechnology, diagnostics and pharmaceutical companies and public and private academic biomedical research organizations. CHI's mission is to advance responsible public policies that foster medical innovation and promote scientific discovery.

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